

Enantioselective Synthesis of Homoallylic Azides and Nitriles via Palladium-Catalyzed Decarboxylative Allylation

Maria Victoria Vita, Paola Caramenti and Jerome Waser.*†

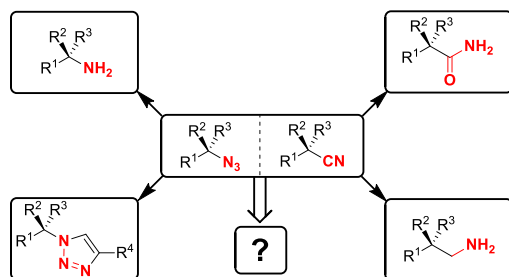
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Supporting Information Placeholder

ABSTRACT: Azides and nitriles are important building blocks for the synthesis of nitrogen-containing bioactive compounds. The first example of enantioselective palladium-catalyzed decarboxylative allylation of α -azido and cyano β -ketoesters is reported. Indanone derivatives were obtained in 50–88% yield/77–97% *ee* and 46–98% yield/78–93% *ee* for azide and nitrile substituents, respectively. The required starting materials were synthesized in one step from ketoesters via electrophilic azidation and cyanation using benziodoxole hypervalent iodine reagents. The products could be easily converted into useful nitrogen-containing building blocks, such as triazoles, amides or α - and β -amino ketones.

Nitrogen-containing functional groups are omnipresent in synthetic and natural bioactive compounds. Among them, azides¹ and nitriles² occupy a privileged position. They are highly useful as non-basic precursors of amines. In addition, they can be transformed in a multitude of other functional groups and can be used in cycloaddition reactions to give a broad range of heterocycles (Figure 1). New methods giving access to nitriles and azides, especially in enantiopure form, are therefore highly useful for both synthetic and medicinal chemistry. Whereas numerous methods are available for the enantioselective synthesis of secondary azides and nitriles, accessing tertiary derivatives is more challenging.

Figure 1. Enantiopure tertiary azides and cyanides: versatile building blocks, but challenging to access.

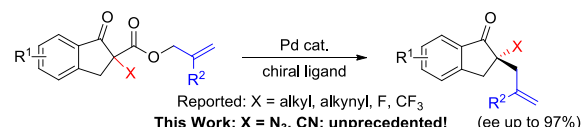


Among the methods used for the enantioselective synthesis of highly substituted stereocenters, the Tsuji-Trost palladium-catalyzed decarboxylative allylation has been especially successful.³ Nevertheless, to the best of our knowledge, this methodology has never been used for the synthesis of homoallylic azides, and there are only racemic examples for cyanides.^{3c,4} This is an important limitation when considering the versatility of these building blocks. In general, the Tsuji-Trost decarboxylation has been only rarely used to synthesize homo-

and bis-homo allylic amines.⁵ In 2015, Stoltz and co-workers, developed in particular an elegant Mannich addition/asymmetric decarboxylative allylation sequence to access bis-homo allylic amines.^{5d}

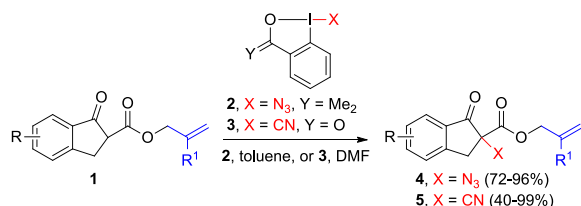
Indan(on)es are privileged structures in bioactive compounds, and nitrogen-substituted derivatives are especially important.⁶ Nevertheless, the enantioselective synthesis of α -azido and cyano indanones has been limited to the azidation of ketoester derivatives⁷ and the conjugate addition or Mannich reaction of α -cyano indanones.⁸ The Tsuji-Trost decarboxylation, although highly successful in the case of other type of substituents,^{3f,9} has never been reported in the case of cyanides and azides (Scheme 1). Herein, we would like to report the first example of highly enantioselective palladium-catalyzed decarboxylative allylation proceeding on cyano- and azido-substituted indanone derivatives. The required substrates were easily synthesized by the azidation or cyanation of ketoesters using hypervalent iodine reagents.

Scheme 1. Enantioselective synthesis of indanones via the Tsuji-Trost decarboxylative allylation.



We started our investigations with the synthesis of the required azido- and cyano- allyl ketoesters **4** and **5**. The desired indanones could be accessed in good yield by the reaction with hypervalent iodine reagents **2** or **3** without any other additives using methods developed in our group¹⁰ and by Chen and co-workers (Scheme 2).¹¹ Unfortunately, the method could not be used to access the corresponding tetralones, due to competitive elimination and aromatization to naphthol derivatives.

Scheme 2. Synthesis of α -azido and cyano allyl ketoesters **4** and **5**.

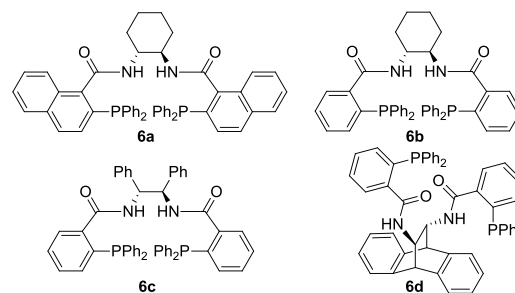


We then turned to the optimization of the decarboxylative allylation for azide **4a** (Table 1).¹² When using Pd(Cp)Cinnamyl as catalyst precursor as in our previous work on the decarboxylative allylation of alkynyl-substituted ketoesters,^{9h} only low conversion was observed. Better results were obtained using Pd₂(dba)₃ with Trost's bisphosphine ligand **6a**, and the desired product **7a** was obtained in 31% yield and 71% *ee*, but 5 mol % catalyst were needed to reach full conversion (Table 1, entry 1).¹² A strong dependence of both yield and enantioselectivity on solvent became apparent (Table 1, entries 2-7). Whereas moderate yields and *ee* were observed in toluene and acetonitrile (Table 1, entries 2 and 3), 93% yield of **7a** was obtained in dichloromethane, albeit at the cost of *ee* (Table 1, entry 4). From the tested ether solvents, THF gave the best result, with 88% yield and 79% *ee* (Table 1, entry 7). Other Trost bisphosphine ligands gave inferior results (Table 1, entries 8-10).¹³ Finally, the enantioselectivity could be improved to 86% by working in more concentrated solution at -20 °C (Table 1, entry 11).

Table 1. Optimization of the decarboxylative allylation of azide **4a**.

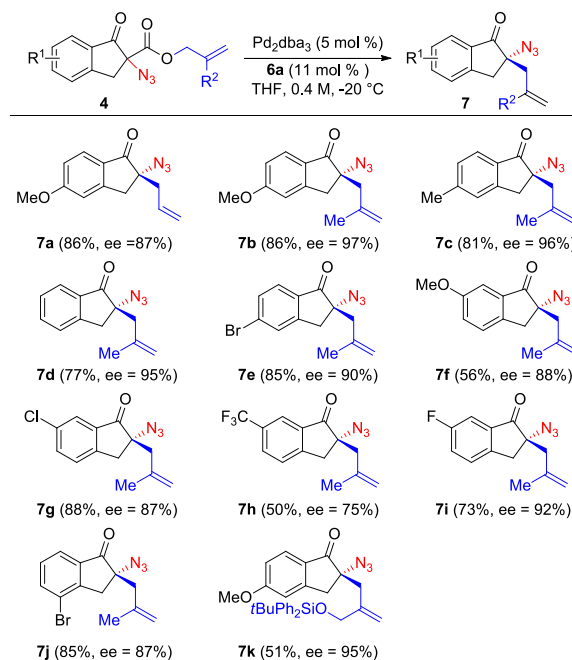
| entry | ligand | solvent | yield (%) ^a | <i>ee</i> (%) ^b |
|----------------|-----------|---------------------------------|------------------------|----------------------------|
| 1 | 6a | MTBE | 31 | 71 |
| 2 | 6a | toluene | 38 | 70 |
| 3 | 6a | CH ₃ CN | 50 | 68 |
| 4 | 6a | CH ₂ Cl ₂ | 93 | 60 |
| 5 | 6a | Et ₂ O | 27 | 71 |
| 6 | 6a | dioxane | 38 | 42 |
| 7 | 6a | THF | 88 | 79 |
| 8 ^c | 6b | THF | 10 | 30 |
| 9 | 6c | THF | <5 | nd |
| 10 | 6d | THF | 15 | 49 |
| 11 | 6a | THF | 88 | 86 ^c |

^aReaction conditions: Substrate **4a** (0.012 mmol), Pd₂(dba)₃ (5 mol %), **6** (11 mol %) and solvent (0.2 M) at 25 °C. The NMR yield is measured in comparison with the internal standard 1,3,5-trimethoxybenzene. ^bObtained by chiral HPLC. ^cAt 0.4 M at -20 °C for 12 h.



The scope of the decarboxylative allylation of azides was then examined (Scheme 3). The use of methallyl substrate **4b** gave the desired product **7b** in improved 97% *ee*. Product **7c** and **7d** bearing either a methyl group or no substituent in C5 position also gave the products in good yield and enantioselectivity. Interestingly, a 5-bromo group was also tolerated, despite the fact that a palladium(0) catalyst is used (product **7e**). Substitution at the C6 position was also possible, although in some cases lower yields and *ee*'s were obtained (products **7f-i**). The decarboxylative allylation was also successful with a 4-bromo substituent (product **7j**). Finally, the use of a more functionalized allyl group bearing a protected alcohol was also possible, as demonstrated by the formation of product **7k** in 51% yield and 95% *ee*.¹⁴

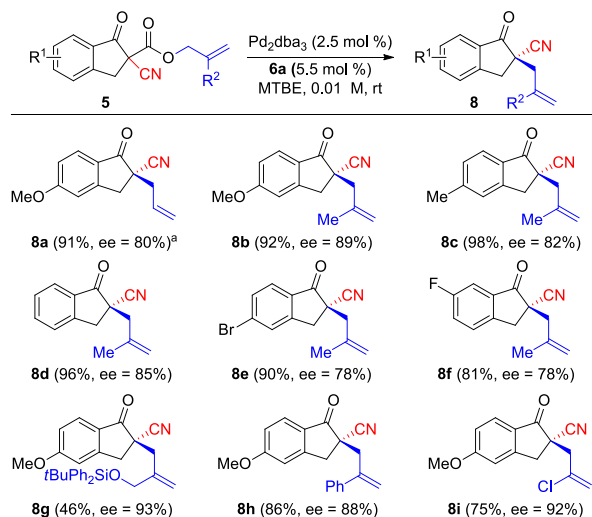
Scheme 3. Scope of the decarboxylative allylation with azides **4**. Reaction conditions: Substrate **4** (0.20 mmol), Pd₂(dba)₃ (5 mol %), **6a** (11 mol %) and THF (0.4 M) at -20 °C, 10-15 h. The isolated yields after column chromatography are given. *ee* are obtained by chiral HPLC.



In the case of cyano substrate **5a**, the conditions used in our previous work for the decarboxylative allylation of α -alkynyl allyl ketoesters (2 mol % Pd(Cp)Cinnamyl, 2.5 mol % **6a**, MTBE, 0.1 M, rt) did not need to be changed extensively.^{9h,12} In fact, working in more diluted conditions (0.01 M) and with higher catalyst/ligand loading (5 and 5.5 mol% respectively) was enough to give the desired allyl cyanides **8a** in 91% yield and 80% *ee* (Scheme 4). For methallyl-based substrates, however, better results were obtained with Pd₂(dba)₃ as catalyst precursor (92% yield and 89% *ee* for **8b**). Irrespectively of the

substitution pattern or electronic properties of the substituents on the benzene ring, the desired methallyl cyanides **8b-f** were obtained in very good yields (81-98%), but the *ee*'s were lower than for azides (78-89%). Modification of the substituent on the alkene was also possible as a protected alcohol, an aryl or a chloride group (products **8g-i**). Protected alcohol **8g** was obtained in 93% *ee*, which is the highest enantioselectivity observed for this class of substrates.

Scheme 4. Scope of the decarboxylative allylation with nitriles **5**. Reaction conditions: Substrate **5** (0.20 mmol), Pd₂(dba)₃ (2.5 mol %), **6a** (5.5 mol %) and THF (0.01 M) at 25 °C, 6-48 h. The isolated yields after column chromatography are given. *ee* are obtained by chiral HPLC. ^aUsing 5 mol % PdCpCinnamyl as catalyst precursor.



The obtained products could be easily transformed into useful nitrogen-containing building blocks (Scheme 5).^{7b,15} Copper-catalyzed [3+2]-cycloaddition of azides **7** with aromatic alkyne **9** gave triazoles **10a-c** in 94-96% yield (Scheme 5, A).^{7b} Staudinger reduction of azide **7e** led to α -amino ketone **11**,^{15a} whereas hydrogenation of nitrile **8b** gave β -amino ketone **12** (Scheme 5, B and C).^{15b} Finally, amide **13** was obtained in 83% yield by hydration of nitrile **8f** in presence of a palladium catalyst (Scheme 5, D).^{15c}

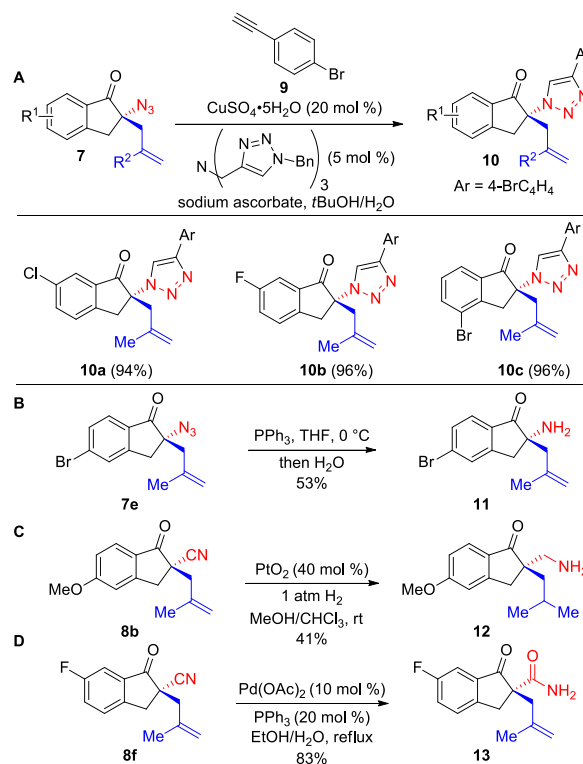
In conclusion, we have reported the first example of enantioselective palladium-catalyzed decarboxylative allylation proceeding next to cyano and azido groups. The reaction proceeded with indanone derivatives in 50-88% yield/77-97% *ee* and 46-98% yield/78-93% *ee* with azide and nitrile substituents, respectively. A broad range of functional groups was tolerated on the benzene ring and the alkene. The required indanone starting materials were obtained by the reaction of benziodoxole hypervalent iodine reagents with ketoesters. The obtained products were easily transformed into useful nitrogen-containing building blocks, such as triazoles, amides and amines.

ASSOCIATED CONTENT

Supporting Information

Experimental procedures and analytical data for all new compounds. This material is available free of charge via the Internet at <http://pubs.acs.org>.

Scheme 5. Modifications of the obtained products.



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M. V. V. and P. C. contributed equally to this work.

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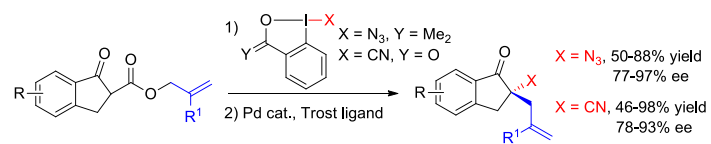
(12) See Supporting Information for a full list of tested conditions for substrates **4a,b** and **5a,b**. A single crystal was grown by slow diffusion of the solution of **8c** in EtOAc/heptane mixture to determine its absolute configuration. Supplementary crystallographic data for this compound have been deposited at the Cambridge Crystallographic Data Centre (CCDC 1418044) and can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif. The absolute configuration of the other substrates was assigned by analogy.

(13) When 'Bu-PHOX (Pfaltz-Helmchen-Williams ligand) was used as ligand in the reaction, no product was obtained in the case of azide-substituted ketoesters. For cyano-substituted ketoesters, the product was obtained in 94% yield, but in racemic form.

(14) Preliminary experiments with linear ketoesters gave less than 10% conversion. Further investigations will be needed for this challenging class of substrates.

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Supporting Information

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Enantioselective Synthesis of Homoallylic Azides and Nitriles *via* Palladium-Catalyzed Decarboxylative Allylation

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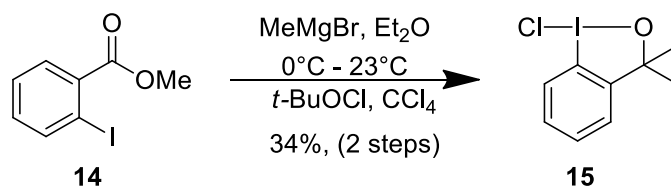
1. General Methods

All reactions were carried out in oven dried glassware under an atmosphere of nitrogen, unless stated otherwise. For quantitative flash chromatography technical grade solvents were used. For flash chromatography for analysis, HPLC grade solvents from Sigma-Aldrich were used. THF, Et₂O, CH₃CN, toluene, hexane and CH₂Cl₂ were dried by passage over activated alumina under nitrogen atmosphere (H₂O content < 10 ppm, *Karl-Fischer* titration). All chemicals were purchased from Acros, Aldrich, Fluka, VWR, Fluorochem, Aplichem or Merck and used without further purification, unless stated otherwise. Chromatographic purification was performed as flash chromatography using Macherey-Nagel silica 40-63, 60 Å, using the solvents indicated as eluent with 0.1-0.5 bar pressure. TLC was performed on Merck silica gel 60 F₂₅₄ TLC aluminium plates and visualized with UV light and anisaldehyde stain. Melting points were measured on a calibrated Büchi B-540 melting point apparatus using open glass capillaries. ¹H-NMR spectra were recorded on a Bruker DPX-400 400 MHz spectrometer in chloroform-d and/or DMSO-d₆. All signals are reported in ppm with the internal chloroform signal at 7.26 ppm or the internal DMSO signal at 2.50 ppm as standard. The data is being reported as (s = singlet, d = doublet, t = triplet, q = quadruplet, qi = quintet, m = multiplet or unresolved, br = broad signal, app = apparent, coupling constant(s) in Hz, integration, interpretation). ¹³C-NMR spectra were recorded with ¹H-decoupling on a Bruker DPX-400 100 MHz spectrometer in chloroform-d and/or DMSO-d₆. All signals are reported in ppm with the internal chloroform signal at 77.0 ppm or the internal DMSO signal at 39.5 ppm as standard. Infrared spectra were recorded on a JASCO FT-IR B4100 spectrophotometer with an ATR PRO410-S and a ZnSe prisma and are reported as cm⁻¹ (w = weak, m = medium, s = strong, br = broad). Gas chromatographic and low resolution mass spectrometric measurements were performed on a Perkin-Elmer Clarus 600 gas chromatographer and mass spectrometer using a Perkin-Elmer Elite fused silica column (length: 30 m, diameter: 0.32 mm) and Helium as carrier gas. High resolution mass spectrometric measurements were performed by the mass spectrometry service of ISIC at the EPFL on a MICROMASS (ESI) Q-TOF Ultima API. All the chiral ligands used in this work are commercially available.

2. Synthesis of Hypervalent Iodine Reagents

2.1 Synthesis of 1-azido-3,3-dimethyl-3-(1*H*)-1,2-benziodoxole (2)

1-Chloro-1,3-dihydro-3,3-dimethyl-1,2-benziodoxole (15)



Following a reported procedure¹ methyl 2-iodobenzoate (**14**) (12 mL, 76 mmol) was dissolved under N_2 atmosphere in dry diethyl ether (400 mL) and then the solution was cooled to 0°C with an ice bath. Methylmagnesium bromide (56.0 mL, 0.168 mol, 2.20 equiv.) was added dropwise and the reaction was stirred for 30 min at 0°C . The reaction mixture was then allowed to warm to room temperature and it was further stirred for 2 h. The reaction was quenched with NH_4Cl in an iced bath. The organic layer was separated and extracted with Et_2O (3 x 100 mL), washed with water (2 x 200 mL), brine (1 x 100 mL) then dried over MgSO_4 . The solvent was removed *in vacuo*.

With no further purification the crude mixture was dissolved in CCl_4 (7 mL) and *tert*-butyl hypochlorite (0.010 L, 92 mmol, 1.2 equiv.) and the reaction mixture was stirred at room temperature. After one hour a yellow precipitate was collected by filtration and washed with hexane (60 mL) to afford compound **15** (7.7 g, 26 mmol, 34% yield) as a yellow solid.

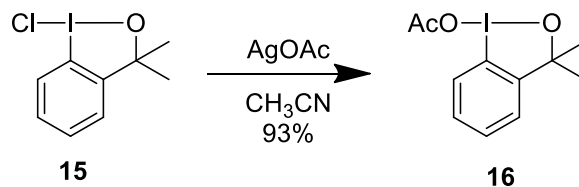
^1H NMR (400 MHz, CDCl_3) δ 8.03 (dd, 1 H, $J = 8.1, 1.1$ Hz, CHAr), 7.55 (m, 2 H, CHAr), 7.17 (dd, 1 H, $J = 7.3, 1.7$ Hz, CHAr), 1.55 (s, 6 H, $(\text{CH}_3)_2$).

^{13}C NMR (101 MHz, CDCl_3) δ 149.5, 131.0, 130.5, 128.4, 126.1, 114.7, 85.2, 29.2.

IR ν_{max} 3729 (w), 3626 (w), 2972 (w), 2924 (w), 2362 (w), 2055 (w), 2018 (w), 1742 (w), 1564 (w), 1464 (w), 1439 (w), 1379 (w), 1378 (w), 1366 (w), 1277 (w), 1276 (w), 1256 (w), 1181 (w), 1154 (m), 1112 (w), 1048 (w), 1003 (w), 982 (w), 943 (m), 866 (m), 808 (w), 790 (w), 789 (w), 762 (s), 745 (w), 724 (w), 718 (w).

The characterization data is in accordance with reported literature values.¹

1-Acetoxy-1,3-dihydro-3,3-dimethyl-1,2-benziodoxole (16)



Following a reported procedure,¹ 1-chloro-1,3-dihydro-3,3-dimethyl-1,2-benziodoxole (**15**) (2.60 g, 8.77 mmol) was dissolved in dry acetonitrile (25 mL) under N_2 atmosphere. The reaction flask was covered with aluminum foils and protected from light. Silver acetate (1.46 g, 8.77 mmol, 1.00 equiv.) was then added in one portion. The reaction mixture was stirred in the dark at room

¹ S. Akai, T. Okuno, M. Egi, T. Takada, H. Tohma, Y. Kita, *Heterocycles* **1996**, 42, 47.

temperature for 16 h. Filtration over a Celite plug and evaporation of the solvent yielded compound **16** (2.6 g, 8.8 mmol, 93%) as a brownish solid.

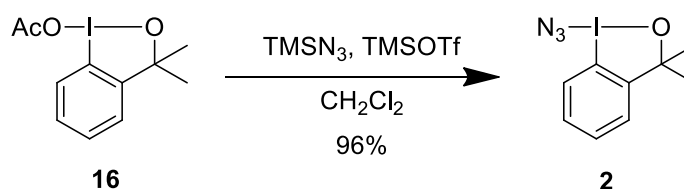
¹H NMR (400 MHz, CDCl₃) δ 7.79 (dd, 1 H, *J* = 8.0, 1.3 Hz, CHAr), 7.47 (m, 2H, CHAr), 7.18 (dd, 1 H, *J* = 7.2, 1.7 Hz, CHAr), 2.11 (s, 3 H, COCH₃), 1.52 (s, 6 H, (CH₃)₂).

¹³C NMR (101 MHz, CDCl₃) δ 177.4, 149.4, 130.4, 130.0, 129.9, 126.2, 115.7, 84.6, 29.2, 21.5.

IR ν_{max} 3099 (w), 3057 (w), 2975 (w), 2930 (w), 2930 (w), 2865 (w), 1740 (w), 1640 (s), 1588 (w), 1566 (w), 1462 (w), 1438 (m), 1363 (s), 1294 (s), 1259 (m), 1158 (m), 1114 (w), 1047 (w), 1033 (w), 1009 (w), 949 (m), 926 (w), 866 (w), 761 (s), 723 (w).

The characterization data is in accordance with reported literature values.¹

1-Azido-3,3-dimethyl-3-(1*H*)-1,2-benziodoxole (**2**)



Caution: This reaction should be carried out behind a safety shield! Following a reported procedure¹ 1-Acetoxy-1,3-dihydro-3,3-dimethyl-1,2-benziodoxole (**16**) (2.30 g, 7.18 mmol) was dissolved in dry CH₂Cl₂ (36 mL) under N₂ atmosphere. The reaction was placed in an iced bath and trimethylsilylazide (0.954 mL, 7.18 mmol, 1.00 equiv.) was added *via* syringe, followed by TMSOTf (0.065 mL, 0.36 mmol, 0.050 equiv.). The reaction was stirred for 15 min then the ice bath was removed and the stirring was continued for 1 h. The solvent was evaporated and the solid obtained was washed with *n*-hexane (2 x 30 mL, HPLC purity) to afford **2** as a yellow crystalline solid (2.10 g, 7.18 mmol, 96%).

¹H NMR (400 MHz, CDCl₃) δ 7.77 (d, 1 H, *J* = 8.0 Hz, CHAr), 7.55 (m, 2 H, CHAr), 7.23 (d, 1 H, *J* = 7.2 Hz, CHAr), 1.53 (s, 7 H, (CH₃)₂).

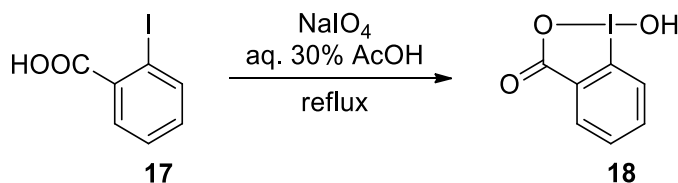
¹³C NMR (101 MHz, CDCl₃) δ 149.2, 130.9, 130.4, 127.8, 126.8, 114.0, 83.2, 29.6.

IR ν_{max} 3254 (w), 3085 (w), 3051 (w), 2976 (w), 2928 (w), 2860 (w), 2486 (w), 2026 (s), 1918 (w), 1764 (w), 1697 (w), 1651 (w), 1589 (w), 1562 (w), 1462 (m), 1428 (m), 1380 (w), 1364 (w), 1312 (w), 1273 (w), 1248 (s), 1182 (w), 1151 (m), 1111 (m), 1031 (w), 1004 (w), 943 (m), 910 (m), 880 (w), 863 (m).

The characterization data is in accordance with reported literature values.¹

2.2 Synthesis of 1-Cyano-1,2-benziodoxol-3-(1*H*)-one (**3**)

1-Hydroxy-1,2-benziodoxol-3-(1*H*)-one (**18**)



Following a reported procedure,² NaIO₄ (25.8 g, 121 mmol, 1.05 eq.) and 2-iodobenzoic acid (**17**) (28.5 g, 115 mmol, 1.00 eq.) were suspended in 30% (v:v) aq. AcOH (175 mL). The mixture was vigorously stirred and refluxed for 4 h. The reaction mixture was then diluted with cold water (500 mL) and allowed to cool to room temperature, while protecting it from light. After 1 h, the crude product was collected by filtration. The crystals were washed with ice water (3 x 100 mL) followed by acetone (3 x 100 mL) and then air-dried in the dark affording **18** (29.3 g, 111 mmol, 96.5%) as a white solid.

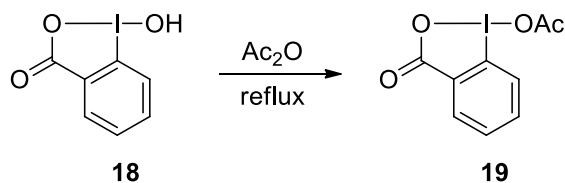
¹H NMR (400 MHz, DMSO-*d*₆) δ 8.04 (s, 1 H, OH), 8.01 (dd, 1 H, *J* = 7.6, 1.5 Hz, Ar*H*), 7.96 (ddd, 1 H, *J* = 8.5, 7.2, 1.5 Hz, Ar*H*), 7.84 (dd, 1 H, *J* = 8.2, 0.7 Hz, Ar*H*), 7.70 (td, 1 H, *J* = 7.3, 1.1 Hz, Ar*H*).

¹³C NMR (100 MHz, (DMSO-*d*₆) δ 167.7, 134.5, 131.5, 131.1, 130.4, 126.3, 120.4.

IR ν_{max} 3083 (w), 3060 (w), 2867 (w), 2402 (w), 1601 (m), 1585 (m), 1564 (m), 1440 (m), 1338 (s), 1302 (m), 1148 (m), 1018 (w), 834 (m), 798 (w), 740 (s), 694 (s), 674 (m), 649 (m).

The characterization data is in accordance with reported literature values.³

1-Acetoxy-1,2-benziodoxol-3-(1*H*)-one (**19**)



Following a reported procedure,⁴ 1-hydroxy-1,2-benziodoxol-3-(1*H*)-one (**18**), 10.3 g, 39.1 mmol, 1.00 equiv.) was suspended in acetic anhydride (35 mL) and heated to reflux for 30 minutes. The resulting clear, slightly yellow solution was slowly let to warm up to room temperature and then cooled to 0 °C for 30 minutes. The white suspension was filtered and the filtrate was again cooled to 0 °C for 30 minutes. The suspension was once again filtered and the combined two batches of solid product were washed with hexane (2 x 20 mL) and dried *in vacuo* affording **19** (10.8 g, 35.3 mmol, 90%) as a white solid.

¹H NMR (CDCl₃, 400 MHz) δ 8.24 (dd, 1 H, *J* = 7.6, 1.6 Hz, Ar*H*), 8.00 (dd, 1 H, *J* = 8.3, 1.0 Hz, Ar*H*), 7.92 (ddd, 1 H, *J* = 8.4, 7.2, 1.6 Hz, Ar*H*), 7.71 (td, 1 H, *J* = 7.3, 1.1 Hz, Ar*H*), 2.25 (s, 3 H, COCH₃).

² L. Kraszkiewicz, L. Skulski, *Arkivoc* **2003**, 120.

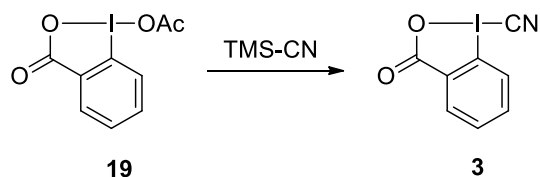
³ J. P. Brand, J. Charpentier, J. Waser, *Angew. Chem. Int. Ed.* **2009**, 48, 9346.

⁴ P. Eisenberger, S. Gischig, A. Togni, *Chem. Eur. J.* **2006**, 12, 2579.

^{13}C NMR (CDCl_3 , 100 MHz) δ 176.5, 168.2, 136.2, 133.3, 131.4, 129.4, 129.1, 118.4, 20.4.

The characterization data is in accordance with reported literature values.⁴

1-Cyano-1,2-benziodoxol-3-(1*H*)-one (3**)**



Following a reported procedure,¹ 1-acetoxy-1,2-benziodoxol-3-(1*H*)-one (**19**), 10.5 g, 34.3 mmol, 1.00 equiv.) was dissolved under nitrogen in dry dichloromethane (80 mL). To the clear colorless solution was added *via* syringe trimethylsilyl cyanide (TMS-CN, 9.20 mL, 68.6 mmol, 2.00 equiv.) over a five minute time period. The reaction mixture was stirred at room temperature and under nitrogen for 72 hours. The resulting thick white suspension was filtered and the solid was washed with hexane (3 x 20 mL) and dried *in vacuo* affording **3** (8.89 g, 32.6 mmol, 95%) as a white solid.

^1H NMR ($\text{DMSO}-d_6$, 400 MHz): δ 8.29 (d, 1 H, J = 8.3 Hz, Ar*H*), 8.13 (dd, 1 H, J = 7.4, 1.7 Hz, Ar*H*), 8.06-7.97 (m, 1 H, Ar*H*), 7.88 (t, 1 H, J = 7.3 Hz, Ar*H*).

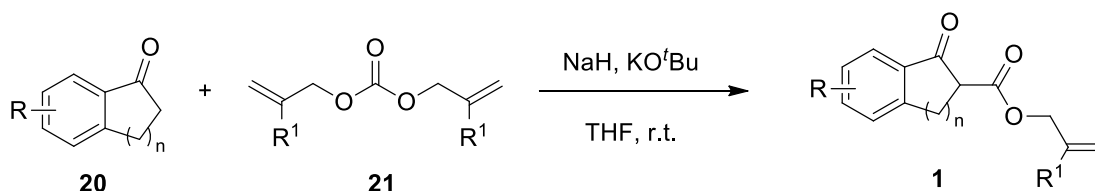
^{13}C NMR ($\text{DMSO}-d_6$, 100 MHz): δ 166.7, 136.5, 132.0, 131.9, 130.2, 127.8, 117.5, 87.9.

IR ν_{max} 3157 (w), 3093 (w), 2160 (w), 1629 (s), 1562 (m), 1439 (m), 1321 (s), 1298 (s), 1148 (m), 839 (m), 747 (s).

The characterization data is in accordance with reported literature values.¹

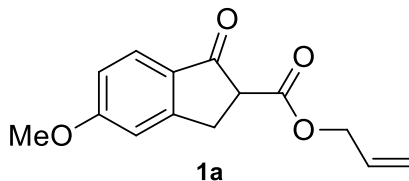
3. Synthesis of starting materials allyl β -keto esters.

General procedure GP1 for the synthesis of β -allyl keto esters.



Following a reported procedure,⁵ potassium *tert*-butoxide (0.05 equiv) was added to a suspension of NaH (2.2 equiv) in diallyl carbonate **21** (2.0 equiv). The ketone **20** (1.0 equiv) was then added dropwise at 0 °C. The reaction was stirred at room temperature and followed by TLC (using the solvent mixture indicated below for the R_f value and UV or *p*-anisaldehyde stain for visualization). Then 1 M HCl was added until the pH of the solution became neutral or slightly acidic. The organic layers were collected and washed with brine (2 x 20 mL), dried over MgSO₄ and concentrated *in vacuo*. The crude product was purified by column chromatography, using the solvent indicated for the R_F value.

Allyl 5-methoxy-1-oxo-2,3-dihydro-1*H*-indene-2-carboxylate (1a)



Following general procedure **GP1**, starting from commercially available 5-methoxy-2,3-dihydro-1*H*-inden-1-one (**20a**) (0.200 g, 1.23 mmol), allyl 5-methoxy-1-oxo-2,3-dihydro-1*H*-indene-2-carboxylate (**1a**) (0.209 g, 0.851 mmol, 69% yield) was obtained as a brown solid.

R_F 0.3 (Pentane:Ethyl Acetate 3:2)

Mp: 53.5-55.9° C.

¹H NMR (400 MHz, Chloroform-*d*) δ 7.70 (d, J = 9.2 Hz, 1H, Ar*H*), 6.96 – 6.89 (m, 2H, Ar*H*), 5.94 (ddt, J = 17.3, 10.5, 5.6 Hz, 1H, CHCH₂), 5.37 (dq, J = 17.2, 1.5 Hz, 1H, CHCH₂), 5.25 (dq, J = 10.5, 1.3 Hz, 1H, CHCH₂), 4.69 (tt, J = 5.7, 1.4 Hz, 2H, CH₂CH), 3.90 (s, 3H, OMe), 3.74 (dd, J = 8.2, 4.0 Hz, 1H, CH), 3.52 (dd, J = 17.3, 4.0 Hz, 1H, CH₂), 3.32 (dd, J = 17.3, 8.2 Hz, 1H, CH₂).

¹³C NMR (101 MHz, Chloroform-*d*) δ 197.4, 169.1, 165.9, 156.7, 131.7, 128.5, 126.4, 118.6, 116.0, 109.6, 66.2, 55.8, 53.5, 30.3.

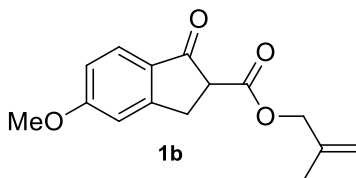
IR ν_{max} 3021 (w), 3013 (w), 2842 (w), 1738 (m), 1705 (s), 1598 (s), 1491 (w), 1337 (w), 1307 (m), 1259 (s), 1224 (w), 1193 (m), 1156 (m), 1149 (m), 1105 (m), 1089 (m), 1025 (m), 989 (m).

The characterization data is corresponding to the reported values.⁶

⁵ M.V. Vita, J. Waser, *Org. Lett.* **2013**, 15, 3246.

⁶ M.V. Vita, J. Waser, *Org. Lett.* **2014**, 16, 5768.

2-Methylallyl 5-methoxy-1-oxo-2,3-dihydro-1H-indene-2-carboxylate (1b)



Following general procedure **GP1**, starting from commercially available 5-methoxy-2,3-dihydro-1H-inden-1-one (**20b**) (1.76 g, 10.9 mmol), 2-methylallyl 5-methoxy-1-oxo-2,3-dihydro-1H-indene-2-carboxylate (**1b**) (2.17 g, 8.34 mmol, 77% yield) was obtained as a yellowish oil.

R_F 0.6 (Pentane:Ethyl Acetate 7:3).

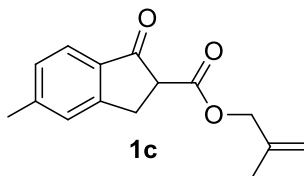
¹H NMR (400 MHz, Chloroform-*d*) δ 7.70 (d, J = 9.1 Hz, 1H, ArH), 6.96-6.92 (m, 2H, ArH), 5.03 (dd, J = 1.6, 0.9 Hz, 1H, CMeCH₂), 4.94 (m, 1H, CMeCH₂), 4.68 – 4.54 (m, 2H, CH₂CMe), 3.90 (s, 3H, OCH₃), 3.78 (dd, 1 H, J = 8.2, 4.0 Hz, CH), 3.55 (dd, 1 H, J = 17.3, 4.0 Hz, CH₂), 3.35 (dd, 1 H, J = 17.3, 8.2 Hz), 1.78 (dd, J = 1.6, 0.9 Hz, 3H, CCH₃).

¹³C NMR (101 MHz, Chloroform-*d*) δ 197.3, 169.1, 165.9, 156.7, 139.6, 128.6, 126.4, 116.0, 113.3, 109.6, 68.7, 55.8, 53.5, 30.3, 19.5.

IR ν_{max} 2978 (w), 2969 (w), 2942 (w), 1740 (m), 1706 (s), 1600 (s), 1306 (w), 1261 (s), 1156 (m), 1090 (m).

The characterization data is corresponding to the reported values.⁶

2-Methylallyl 5-methyl-1-oxo-2,3-dihydro-1H-indene-2-carboxylate (1c)



Following general procedure **GP1**, starting from commercially available 5-methyl-2,3-dihydro-1H-inden-1-one (**20c**) (0.50 g, 3.4 mmol), 2-methylallyl 5-methyl-1-oxo-2,3-dihydro-1H-indene-2-carboxylate (**1c**) (0.60 g, 2.3 mmol, 67% yield) was obtained as a orange oil.

R_F 0.66 (Pentane:Ethyl Acetate 4:1).

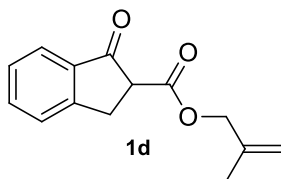
¹H NMR (400 MHz, Chloroform-*d*) δ 7.66 (d, J = 7.9 Hz, 1H, ArH), 7.30 (s, 1H, ArH), 7.20 (d, J = 7.9 Hz, 1H, ArH), 5.02 (s, 1H, CMeCH₂), 4.96 – 4.89 (m, 1H, CMeCH₂), 4.69 – 4.52 (m, 2H, CH₂CMe), 3.75 (dd, J = 8.2, 4.0 Hz, 1H, CH), 3.60 – 3.44 (m, 1H, CH₂), 3.33 (dd, J = 17.2, 8.2 Hz, 1H, CH₂), 2.45 (s, 3H, CH₃), 1.77 (s, 3H, CH₃).

¹³C NMR (101.00 MHz, Chloroform-*d*) δ 198.8, 169.0, 154.1, 146.8, 139.6, 133.0, 129.1, 126.9, 124.5, 113.3, 68.7, 53.5, 30.2, 22.2, 19.5.

IR ν_{max} 2933 (w), 1741 (m), 1712 (s), 1609 (m), 1269 (m), 1233 (m), 1196 (m), 1155 (m), 910 (w), 909 (w).

HRMS (ESI) calcd for C₁₅H₁₇O₃⁺ [M+H]⁺ 245.1172; found 245.1177.

2-Methylallyl 1-oxo-2,3-dihydro-1H-indene-2-carboxylate (1d)



Following general procedure **GP1**, starting from commercially available 2,3-dihydro-1H-inden-1-one (**20d**) (0.500 g, 3.78 mmol), 2-methylallyl 1-oxo-2,3-dihydro-1H-indene-2-carboxylate (**1d**) (0.653 g, 2.84 mmol, 75% yield) was obtained as a purple liquid.

R_F 0.3 (Pentane:Ethyl Acetate 3:2).

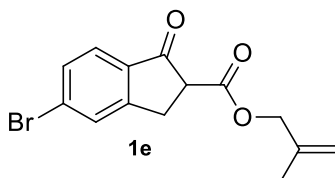
¹H NMR (400 MHz, Chloroform-*d*) (Ketone/Enol 1:0.2) *Ketone*: δ 7.78 (d, *J* = 7.7 Hz, 1H, Ar*H*), 7.63 (dd, *J* = 8.1, 6.8 Hz, 1H, Ar*H*), 7.51 (d, *J* = 7.7 Hz, 1H, Ar*H*), 7.43 – 7.36 (m, 1H, Ar*H*), 5.05 – 4.91 (m, 2H, CMeCH₂), 4.72 – 4.52 (m, 2H, CH₂CMe), 3.77 (dd, *J* = 8.3, 4.1 Hz, 1H, CHCH₂), 3.64 – 3.52 (m, 1H, CH₂CH), 3.40 (dd, *J* = 17.2, 8.2 Hz, 1H, CH₂CH), 1.78 (d, *J* = 1.4 Hz, 3H, CMe). *Enol*: δ 7.65 (m, 1H, Ar*H*), 7.47 (d, *J* = 1.3 Hz, 1H, Ar*H*), 7.44 (dd, *J* = 7.3, 1.4 Hz, 1H, Ar*H*), 7.39 (m, 1H, Ar*H*), 5.05 (d, *J* = 1.5 Hz, 1H, CMeCH₂), 4.98 (t, *J* = 1.4 Hz, 1H, CMeCH₂), 4.69 (s, 2H, CH₂CMe), 3.56 (s, 2H, CH₂), 1.82 (s, 3H, CMe).

¹³C NMR (101.00 MHz, Chloroform-*d*) *Ketone*: δ 199.3, 168.8, 153.5, 139.5, 135.4, 135.3, 127.9, 126.6, 124.7, 113.4, 68.8, 53.3, 30.3, 19.5. *Enol*: δ 143.2, 140.0, 136.9, 129.5, 126.9, 124.8, 120.8, 112.8, 102.2, 67.1, 32.5, 29.7.⁷

IR ν_{max} 1746 (s), 1716 (s), 1464 (w), 1328 (w), 1314 (w), 1300 (w), 1286 (w), 1274 (w), 1248 (w), 1207 (m), 1186 (m), 1155 (m), 1128 (w), 991 (w), 990 (w), 917 (w), 908 (w), 765 (m).

The characterization data is corresponding to the reported values.⁶

2-Methylallyl 5-bromo-1-oxo-2,3-dihydro-1H-indene-2-carboxylate (1e)



Following general procedure **GP1**, starting from commercially available 5-bromo-2,3-dihydro-1H-inden-1-one (**20e**) (0.500 g, 2.37 mmol), 2-methylallyl 5-bromo-1-oxo-2,3-dihydro-1H-indene-2-carboxylate (**1e**) (0.501 g, 1.62 mmol, 68% yield) was obtained as a yellow solid.

R_F 0.3 (Pentane:Ethyl acetate 3:2).

Mp: 58.2-61.9 °C.

⁷ 2C in the enol are missing, one possibly the ester.

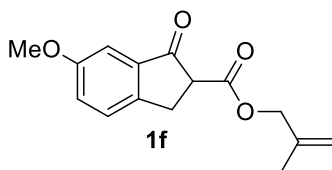
¹H NMR (400 MHz, Chloroform-*d*) Ketone/Enol form (1.5:1) *Ketone*: δ 7.69 (d, *J* = 1.6 Hz, 1H, Ar*H*), 7.63 (d, *J* = 8.2 Hz, 1H, Ar*H*), 7.56 – 7.51 (m, 1H, Ar*H*), 5.02 (s, 1H, CCH₂), 4.95 (s, 1H, CCH₂), 4.68 – 4.54 (m, 2H, CH₂C), 3.77 (dd, *J* = 8.3, 4.1 Hz, 1H, CH), 3.54 (dd, *J* = 17.4, 4.0 Hz, 1H, CH₂), 3.37 (dd, *J* = 17.5, 8.3 Hz, 1H, CH₂), 1.79 – 1.76 (m, 3H, CCH₃). *Enol*: δ 10.31 (s, 1H, OH), 7.62 (s, 1H, Ar*H*), 7.52 – 7.50 (m, 2H, Ar*H*), 5.05 – 5.03 (m, 1H, CCH₂), 4.98 (t, *J* = 1.4 Hz, 1H, CCH₂), 4.69 (s, 2H, CH₂C), 3.53 (s, 2H, CH₂), 1.82 (t, *J* = 1.1 Hz, 3H, CCH₃).

¹³C NMR (101.00 MHz, Chloroform-*d*) δ 198.0, 168.3, 155.1, 144.9, 139.9, 139.4, 135.9, 134.1, 131.6, 131.0, 130.2, 129.9, 128.1, 125.8, 124.0, 122.0, 113.5, 113.0, 102.5, 68.9, 67.3, 53.3, 32.4, 30.0, 19.5, 19.5. ⁸

IR ν_{\max} 2977 (w), 2940 (w), 2934 (w), 1742 (m), 1717 (s), 1652 (m), 1620 (m), 1597 (m), 1562 (m), 1418 (m), 1316 (m), 1288 (m), 1260 (m), 1211 (s), 1200 (s), 1179 (s), 1159 (m), 1133 (m), 1101 (m), 992 (m), 911 (m).

The characterization data is corresponding to the reported values.⁶

2-Methylallyl 6-methoxy-1-oxo-2,3-dihydro-1*H*-indene-2-carboxylate (1f)



Following general procedure **GP1**, starting from commercially available 6-methoxy-2,3-dihydro-1*H*-inden-1-one (**20f**) (0.30 g, 1.9 mmol), 2-methylallyl 6-methoxy-1-oxo-2,3-dihydro-1*H*-indene-2-carboxylate (**1f**) (0.30 g, 1.2 mmol, 66% yield) was obtained as a pink oil.

R_F 0.43 (pentane: ethyl acetate 8:2).

¹H NMR (400 MHz, Chloroform-*d*) (Ketone/Enol 1:0.2) *Ketone* δ 7.39 (dq, *J* = 8.3, 0.8 Hz, 1H, Ar*H*), 7.22 (dd, *J* = 8.3, 2.6 Hz, 1H, Ar*H*), 7.19 (d, *J* = 2.5 Hz, 1H, Ar*H*), 5.03 (s, 1H, CMeCH₂), 4.94 (s, 1H, CMeCH₂), 4.68 – 4.52 (m, 2H, CH₂CMe), 3.83 (s, 3H, OMe), 3.79 (dd, *J* = 8.1, 3.9 Hz, 1H, CH), 3.48 (ddd, *J* = 17.0, 4.0, 1.0 Hz, 1H, CH₂), 3.32 (ddd, *J* = 16.9, 8.1, 0.9 Hz, 1H, CH₂), 1.78 (s, 3H, CH₃). *Enol* δ 10.38 (s, 1H, OH), 7.35 (dd, *J* = 8.3, 0.7 Hz, 1H, Ar*H*), 7.16 (d, *J* = 2.4 Hz, 1H, Ar*H*), 7.00 (dd, *J* = 8.3, 2.5 Hz, 1H, Ar*H*), 5.05 – 5.04 (m, 1H, CMeCH₂), 4.97 (ddd, *J* = 2.5, 1.7, 1.0 Hz, 1H, CMeCH₂), 4.69 (s, 2H, CH₂CMe), 3.86 (s, 3H, OMe), 3.50 (s, 2H, CH₂), 1.82 (dd, *J* = 1.6, 0.9 Hz, 3H, CH₃).

¹³C NMR (101 MHz, Chloroform-*d*) *Ketone* δ 199.3, 168.9, 159.7, 146.5, 139.5, 136.5, 127.2, 125.0, 113.4, 105.7, 68.8, 55.7, 54.0, 29.7, 19.5. *Enol* δ 159.2, 140.0, 138.0, 135.5, 125.4, 117.2, 112.8, 104.5, 103.3, 67.1, 55.6, 31.8, 19.5. ⁹

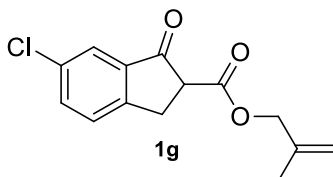
IR ν_{\max} 2942 (w), 2941 (w), 1740 (m), 1711 (s), 1493 (w), 1438 (w), 1277 (m), 1229 (m), 1211 (m), 1187 (w), 1186 (w), 1156 (m), 1029 (w), 910 (s), 733 (s).

HRMS (ESI) calcd for C₁₅H₁₆NaO₄⁺ [M+Na]⁺ 283.0941; found 283.0940.

⁸ Aromatic C of the enol form are not resolved.

⁹ 2 C in the aromatic region of the enol form are not resolved.

2-Methylallyl 6-chloro-1-oxo-2,3-dihydro-1H-indene-2-carboxylate (1g)



Following general procedure **GP1**, starting from commercially available 6-chloro-2,3-dihydro-1H-inden-1-one (**20g**) (0.50 g, 3.0 mmol), 2-methylallyl 6-chloro-1-oxo-2,3-dihydro-1H-indene-2-carboxylate (**1g**) (0.59 g, 2.2 mmol, 74% yield) was obtained as pink solid.

R_F 0.3 (Pentane:Ethyl Acetate 3:2).

Mp: 71.5-73.7° C.

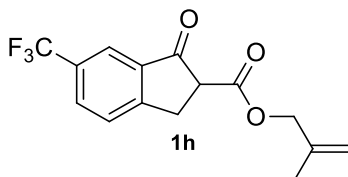
¹H NMR (400 MHz, Chloroform-*d*) Ketone/enol ratio (1:0.5) *Ketone* δ 7.73 (d, J = 2.1 Hz, 1H, ArH), 7.58 (dd, J = 8.2, 2.1 Hz, 1H, ArH), 7.39 (d, J = 1.3 Hz, 1H, ArH), 5.04 – 5.00 (s, 1H, CCH₂), 4.97 – 4.93 (s, 1H, CCH₂), 4.68 – 4.52 (m, 2H, CH₂C), 3.80 (dd, J = 8.2, 4.0 Hz, 1H, CH), 3.54 (dd, J = 17.3, 4.0, 1H, CH₂), 3.36 (dd, J = 17.4, 8.1 Hz, 1H, CH₂), 1.77 (s, 3H, CCH₃). *Enol*: δ 10.25 (s, 1H, OH), 7.62 (s, 1H, ArH), 7.45 (d, J = 8.1 Hz, 2H, ArH), 5.05 (s, 1H, CCH₂), 4.98 (s, 1H, CCH₂), 4.69 (s, 2H, CH₂C), 3.54 (s, 2H, CH₂), 1.82 (d, J = 1.5 Hz, 3H, CCH₃).

¹³C NMR (101.00 MHz, Chloroform-*d*) δ 198.0, 168.3, 151.6, 141.2, 139.9, 139.4, 138.6, 136.8, 135.5, 134.3, 133.1, 129.4, 127.7, 125.8, 124.4, 120.9, 113.5, 113.0, 103.7, 69.0, 67.3, 53.7, 32.3, 29.9, 19.5, 19.4.¹⁰

IR ν_{max} 2975 (w), 2935 (w), 2861 (w), 2860 (w), 1745 (m), 1720 (s), 1652 (m), 1620 (m), 1592 (m), 1568 (m), 1339 (m), 1255 (s), 1201 (s), 1187 (s), 1166 (m), 1131 (m), 1107 (m), 907 (w), 777 (w).

The characterization data is corresponding to the reported values.⁶

2-Methylallyl 6-trifluoromethyl-1-oxo-2,3-dihydro-1H-indene-2-carboxylate (1h)



Following general procedure **GP1**, starting from commercially available 6-(trifluoromethyl)-2,3-dihydro-1H-inden-1-one (**20h**) (0.23 mL, 1.5 mmol), 2-methylallyl 1-oxo-6-(trifluoromethyl)-2,3-dihydro-1H-indene-2-carboxylate (**1h**) (0.32 g, 1.1 mmol, 71% yield) was obtained as pink solid.

¹⁰ 2 aromatic C of the enol form are not resolved.

R_F 0.25 (Pentane:Ethyl Acetate 9:1).

Mp: 56.7-59.2° C.

¹H NMR (400 MHz, Chloroform-*d*) (Ketone/enol 0.5:1) *Ketone* δ 8.05 (d, *J* = 1.7 Hz, 1H, ArH), 7.66 (d, *J* = 8.2 Hz, 2H, ArH), 5.05 – 5.02 (m, 1H, CCH₂), 4.96 (t, *J* = 1.5 Hz, 1H, CCH₂), 4.65 (s, 1H, CH₂CMe), 4.58 (d, *J* = 13.0 Hz, 1H, CH₂CMe), 3.85 (dd, *J* = 8.3, 4.0 Hz, 1H, CH₂), 3.71 – 3.64 (m, 1H, CH₂), 3.46 (dd, *J* = 17.7, 7.9 Hz, 1H, CH₂), 1.81 – 1.76 (m, 3H, CH₂CMe). *Enol*: δ 10.29 (s, 1H, OH), 7.93 – 7.90 (m, 1H, ArH), 7.88 (dd, *J* = 8.2, 1.7 Hz, 1H, ArH), 7.59 (d, *J* = 7.9 Hz, 1H, ArH), 5.06 (p, *J* = 1.2 Hz, 1H, CMeCH₂), 5.00 (q, *J* = 1.3 Hz, 1H, CMeCH₂), 4.71 (s, 2H, CH₂CMe), 3.63 (s, 2H, CH₂), 1.86 – 1.80 (m, 3H, CCH₃).

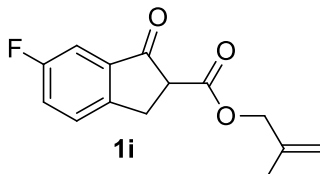
¹³C NMR (101 MHz, Chloroform-*d*) δ 198.0, 168.6, 168.5, 168.1, 156.6, 146.5, 139.8, 139.3, 137.6, 135.7, 131.9 (q, *J* = 3.6 Hz), 130.7 (t, *J* = 33.1 Hz), 129.7 (d, *J* = 32.4 Hz), 127.4, 126.10 (q, *J* = 3.8 Hz), 125.1, 124.2 (q, *J* = 272.2 Hz), 123.6 (q, *J* = 273 Hz), 122.0 (q, *J* = 4.0 Hz), 117.9 (q, *J* = 3.9 Hz), 113.6, 113.1, 103.7, 69.1, 67.4, 53.5, 32.8, 30.4, 19.5, 19.4.

¹⁹F NMR (376 MHz, CDCl₃) δ -62.1, -62.6.

IR ν_{max} 2944 (w), 1724 (m), 1657 (m), 1324 (s), 1269 (s), 1254 (m), 1215 (m), 1189 (m), 1164 (s), 1128 (s), 1103 (s), 909 (m).

The characterization data is corresponding to the reported values.⁶

2-Methylallyl 6-fluoro-1-oxo-2,3-dihydro-1*H*-indene-2-carboxylate (1i**)**



Following general procedure **GP1**, starting from commercially available 5-fluoro-2,3-dihydro-1*H*-inden-1-one (**20i**) (0.50 g, 3.3 mmol), 2-methylallyl 5-fluoro-1-oxo-2,3-dihydro-1*H*-indene-2-carboxylate (**1i**) (0.50 g, 1.9 mmol, 57% yield) was obtained as a brown oil.

R_F 0.3 (Dichloromethane:Pentane 3:2).

¹H NMR (400 MHz, Chloroform-*d*) (Ketone/Enol 1:0.4) *Ketone* δ 7.48 (dd, *J* = 8.4, 4.4 Hz, 1H, ArH), 7.41 (dd, *J* = 7.3, 2.4 Hz, 1H, ArH), 7.36 (dd, *J* = 8.5, 2.6 Hz, 1H, ArH), 5.03 (s, 1H, CCH₂), 4.95 (s, 1H, CCH₂), 4.68 – 4.54 (m, 2H, OCH₂), 3.82 (dd, *J* = 8.2, 4.0 Hz, 1H, CH), 3.58 – 3.49 (m, 1H, CH₂), 3.36 (ddt, *J* = 17.1, 8.2, 1.2 Hz, 1H, CH₂), 1.78 (t, *J* = 1.1 Hz, 3H, CH₃). *Enol* δ 7.39 (m, 1H, ArH), 7.34 – 7.30 (m, 1H, ArH), 7.12 (ddd, *J* = 9.3, 8.3, 2.5 Hz, 1H, ArH), 5.05 (t, *J* = 1.2 Hz, 1H, CCH₂), 4.98 (t, *J* = 1.4 Hz, 1H, CCH₂), 4.70 (s, 2H, OCH₂C), 3.51 (s, 2H, CH₂), 1.82 (t, *J* = 1.1 Hz, 3H, CH₃).

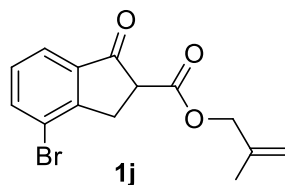
¹³C NMR (101 MHz, Chloroform-*d*) *Ketone*: δ 198.3, 168.4, 162.5 (d, *J* = 248.8 Hz), 148.9 (d, *J* = 2.2 Hz), 139.4, 137.0 (d, *J* = 7.7 Hz), 127.9 (d, *J* = 8.0 Hz), 123.2 (d, *J* = 23.8 Hz), 113.5, 110.5 (d, *J* = 22.2 Hz), 68.9, 54.1, 29.8, 19.4. *Enol*: δ 162.3 (d, *J* = 244.7 Hz), 148.9, 139.9,

138.7, 138.5 (d, $J = 2.4$ Hz), 125.8 (d, $J = 8.8$ Hz), 116.6 (d, $J = 23.3$ Hz), 113.0, 107.7 (d, $J = 23.8$ Hz), 104.1, 67.3, 32.0, 19.5.¹¹

IR ν_{\max} 3075 (w), 2937 (w), 1742 (m), 1718 (s), 1655 (m), 1577 (m), 1488 (m), 1262 (s), 1198 (s), 1147 (s).

HRMS (ESI) calcd for $C_{14}H_{14}FO_3^+$ $[M+H]^+$ 249.0921; found 249.0927

2-Methylallyl 4-bromo-1-oxo-2,3-dihydro-1H-indene-2-carboxylate (1j)



Following general procedure **GP1**, starting from commercially available 4-bromo-2,3-dihydro-1H-inden-1-one (**20j**) (0.50 g, 2.4 mmol), 2-methylallyl 4-bromo-1-oxo-2,3-dihydro-1H-indene-2-carboxylate (**1j**) (0.60 g, 2.0 mmol, 83% yield) was obtained as a pink solid.

R_F 0.3 (Pentane:Ethyl Acetate 9:1).

Mp: 51-54° C.

¹H NMR (400 MHz, Chloroform-*d*) (Ketone/Enol 1:0.5) *Ketone* δ 7.90 (dd, $J = 7.8, 0.9$ Hz, 1H, ArH), 7.41 (dd, $J = 8.9, 7.0$ Hz, 1H, ArH), 7.38 (d, $J = 9.5$ Hz, 1H, ArH), 5.14 (t, $J = 1.3$ Hz, 1H, CMeCH₂), 5.06 (s, 1H, CMeCH₂), 4.77 (d, $J = 13.0$ Hz, 1H, CH₂CMe), 4.69 (d, $J = 13.0$ Hz, 1H, CH₂CMe), 3.91 (dd, $J = 8.3, 4.0$ Hz, 1H, CH), 3.60 (m, 1H, CH₂), 3.44 (dd, $J = 17.8, 8.3$ Hz, 1H, CH₂), 1.89 (t, $J = 1.1$ Hz, 3H, CH₃). *Enol* δ 10.40 (s, 1H, OH), 7.83 (d, $J = 7.5$ Hz, 1H, ArH), 7.68 (m, 2H, ArH), 5.16 (t, $J = 1.4$ Hz, 1H, CMeCH₂), 5.12 – 5.07 (m, 1H, CMeCH₂), 4.81 (s, 2H, CH₂CMe), 3.62 (s, 2H, CH₂), 1.94 (d, $J = 1.3$ Hz, 3H, CH₃).

¹³C NMR (101.00 MHz, Chloroform-*d*) *Ketone*: δ 198.5, 168.3, 138.2, 132.5, 129.6, 128.8, 123.51, 119.9, 113.6, 113.1, 69.0, 53.2, 31.4, 19.5. *Enol*: δ 153.2, 143.1, 139.9, 139.4, 138.5, 137.2, 122.0, 119.7, 102.9, 67.4, 34.1, 19.5.¹²

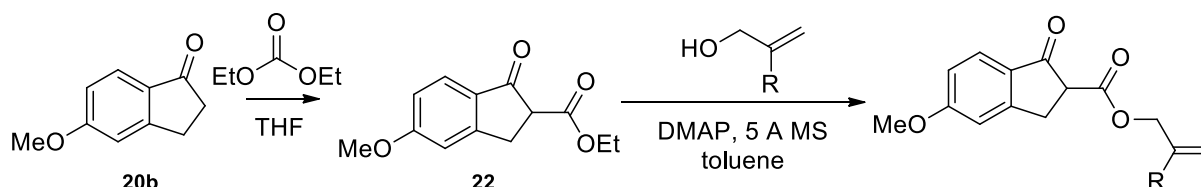
IR ν_{\max} 3082 (w), 2979 (w), 1748 (s), 1723 (s), 1656 (m), 1563 (m), 1456 (m), 1262 (s), 1235 (s), 1188 (s), 910 (m), 772 (m).

HRMS (ESI) calcd for $C_{14}H_{13}^{79}BrNaO_3^+$ $[M+Na]^+$ 330.9940; found 330.9943

¹¹ 1C in the enol form is not resolved.

¹² Two C of the aromatic region of the enol form are not resolved.

3.1 Synthesis of substrates **1k**, **1l** and **1m**.



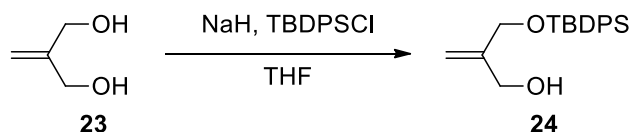
Ethyl 5-methoxy-1-oxo-2,3-dihydro-1H-indene-2-carboxylate (26**)**

Following a reported procedure,¹³ potassium *tert*-butoxide (6.9 mg, 0.062 mmol, 0.0050 equiv.) was added to a suspension of NaH (1.1 g, 27 mmol, 2.2 equiv.) and diethyl carbonate (7.5 mL, 62 mmol, 5.0 equiv.). Commercially available 5-Methoxy-2,3-dihydro-1H-inden-1-one (**20b**) (2.0 g, 12 mmol) was then added carefully at 0 °C. The reaction was stirred at room temperature and followed by TLC. Then 1 M HCl was added until the pH of the solution became neutral or slightly acidic. The organic layers were collected and washed with brine (2 x 20 mL), dried over MgSO₄ and concentrated in vacuum. The crude product was purified by column chromatography (7:3 Pentane/Ethyl acetate) to afford the pure compound **22** (2.8 g, 12 mmol, 96% yield) as a yellow resin.

¹H NMR (400 MHz, Chloroform-*d*) δ 7.70 (d, *J* = 9.1 Hz, 1H, ArH), 6.94 – 6.89 (m, 2H, ArH), 4.29 (dd, 1H, *J* = 7.2, 0.9 Hz, CH₂CH₃), 4.25 (dd, 1H, *J* = 7.2, 0.8 Hz, CH₂CH₃), 3.89 (s, 3H, OMe), 3.70 (dd, *J* = 8.2, 3.9 Hz, 1H, CH), 3.50 (ddt, *J* = 17.2, 4.0, 1.0 Hz, 1H, CH₂), 3.33 (dd, 1H, *J* = 17.3, 8.1 Hz, CH₂), 1.31 (t, *J* = 7.1 Hz, 3H, CH₂CH₃).

The characterization data for compounds **22** is corresponding to the reported values.¹³

2-(((*tert*-Butyldiphenylsilyl)oxy)methyl)prop-2-en-1-ol (24**)**



Following a reported procedure,¹⁴ 2-methylenepropane-1,3-diol **23** (0.50 mL, 6.1 mmol) was dissolved in THF (15 mL), the solution was cooled at 0 °C before the addition of NaH (0.25 g 60% dispersed in mineral oil, 6.1 mmol, 1.0 equiv.). After 1 h, TBDPSCI (1.6 mL, 6.1 mmol, 1.0 equiv.) was added and the reaction was stirred at room temperature for 18-20 h. The solution was then cooled to 0 °C and quenched with iced water and then extracted with diethyl ether (3 x 50 mL). The organic layers are recombined and washed with a saturated solution of K₂CO₃ (50 mL), brine (50 mL) and dried over Na₂SO₄. Evaporation of the solvent afforded compound **24** (2.0 g, 6.1 mmol, 99% yield) as a colorless oil which was used without further purification for the transesterification.

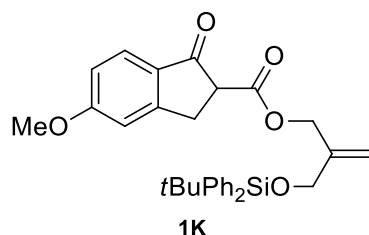
¹H NMR (400 MHz, Chloroform-*d*) δ 7.82 – 7.62 (m, 4H, Ph), 7.52 – 7.30 (m, 6H, Ph), 5.16 (s, 1H, CCH₂), 5.12 (s, 1H, CCH₂), 4.26 (s, 2H, CH₂C), 4.20 – 4.16 (m, 2H, CH₂C), 1.08 (s, 9H, *t*Bu).

The characterization data for compounds **24** is corresponding to reported values.¹⁴

¹³ A. Martinez, M. Fernandez, J. Estevez, J.R. Estevez, L. Castaldo, *Tetrahedron Lett.* **2005**, 61, 1353.

¹⁴ F. Russo, F. Wangsell, J. Saevmarker, M. Jacobsson, M. Larhed, *Tetrahedron* **2009**, 65, 10047.

2-(((tert-Butyldiphenylsilyl)oxy)methyl)allyl 5-methoxy-1-oxo-2,3-dihydro-1H-indene-2-carboxylate (1k)



Substrate **1k** was synthesized following a reported procedure,¹³ in a 2 neck 50 mL flask compound **22** (0.30 g, 1.3 mmol) DMAP (0.16 g, 1.3 mmol, 1.0 equiv.), 2-(((tert-butyl(diphenyl)silyl)methyl)prop-2-en-1-ol (**24**) (0.44 g, 1.4 mmol, 1.1 equiv.) and c.a 200-300 mg of activated 5 Å MS were suspended in dry toluene (6.5 mL, 0.2 M) and the reaction mixture heated to reflux till disappearance of the starting material (TLC Pentane:Ethyl Acetate 4:1). The reaction was quenched with 1 M HCl and water; the aqueous layer was extracted with diethyl ether (2 x 30 mL). The organic layers were collected and washed with NaHCO₃ and brine and then dried over MgSO₄. Filtration and removal of the solvent under reduced pressure afforded the crude product which was purified by column chromatography (Pentane:Ethyl Acetate 4:1). The title compound **1k** (0.28 g, 0.53 mmol, 42% yield) was obtained as a colorless oil

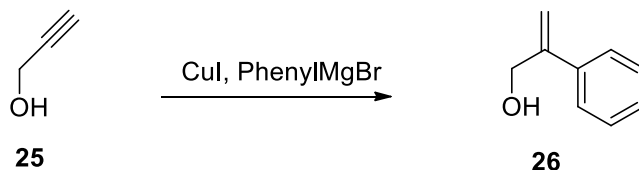
¹H NMR (400 MHz, Chloroform-*d*) δ 7.71 – 7.64 (m, 4H, *Ph*+ *ArH*), 7.46 – 7.33 (m, 7H, *Ph*), 6.91 (ddd, *J* = 8.6, 1.9, 1.1 Hz, 1H, *ArH*), 6.90 – 6.88 (m, 1H, *ArH*), 5.30 (s, 1H, CMeCH₂), 5.22 (s, 1H, CMeCH₂), 4.77 – 4.67 (m, 2H, CH₂CMe), 4.21 (dt, *J* = 2.2, 1.4 Hz, 2H, CH₂OTBDPS), 3.89 (s, 3H, OMe), 3.68 (dd, *J* = 8.2, 4.0 Hz, 1H, CH), 3.44 (dd, *J* = 17.3, 4.1 Hz, 1H, CH₂), 3.33 – 3.21 (m, 1H, CH₂), 1.05 (s, 9H, *t*Bu).

¹³C NMR (101 MHz, Chloroform-*d*) δ 197.2, 169.0, 165.9, 156.6, 142.3, 135.5, 133.4, 129.7, 128.5, 127.7, 126.4, 115.9, 113.1, 109.6, 65.6, 64.5, 55.8, 53.4, 30.3, 26.8, 19.3.

IR ν_{\max} 2956 (w), 2932 (w), 2858 (w), 1744 (w), 1743 (w), 1709 (s), 1600 (s), 1261 (s), 1111 (s), 1090 (m).

The characterization data is corresponding to the reported values.⁶

2-Phenylprop-2-en-1-ol (26)



Following a reported procedure,¹⁵ phenylmagnesium bromide (69 mL, 90 mmol, 3 equiv.) was added dropwise to a cooled (-78 °C) mixture of prop-2-yn-1-ol (**25**) (1.2 mL, 30 mmol) and copper(I) iodide (2.86 g, 15.0 mmol, 0.5 equiv.) in THF (40.0 mL). The resultant reaction

¹⁵S. M. Smith, G.L. Hoang, R. Pal, M. O. B. Khaled, L. S. Pelter, X.C. Zeng, J. M. Takacs, *Chem. Commun.*, **2012**, 48, 12180.

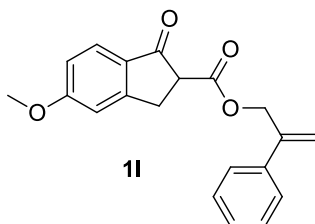
mixture was allowed to slowly warm to room temperature and stirred for 16 h. The reaction mixture was then cooled to 0 °C and quenched with sat. ammonium chloride (20 mL) and then extracted with diethyl ether (3 x 30 mL). The combined organic extracts were dried over anhydrous Na₂SO₄ and then concentrated under reduced pressure. Flash chromatography over silica gel (Hexane:EtOAc 80:20) afforded the desired compound **26** (3.1 g, 23 mmol, 77% yield) as a colorless oil.

R_F 0.4 (Hexanes:Ethyl Acetate 75:25).

¹H NMR (400 MHz, Chloroform-*d*) δ 7.55–7.45 (m, 2H, *Ph*), 7.45– 7.30 (m, 3H, *Ph*), 5.50 (s, 1H, CCH₂), 5.39 (s, 1H, CCH₂), 4.55 (s, 2H, CH₂C), 2.28 (br, 1H, OH).

The characterization data for compounds **26** corresponded to the reported values.¹⁵

2-Phenylallyl 5-methoxy-1-oxo-2,3-dihydro-1*H*-indene-2-carboxylate (11)



Substrate **11** was synthesized following a reported procedure,¹³ in a 2 neck 25 mL flask compound **22** (0.368 g, 2.00 mmol), DMAP (0.244 g, 2.00 mmol, 1.0 equiv.), 2-phenylprop-2-en-1-ol (**26**) (0.282 g, 2.10 mmol, 2.1 equiv.) and c.a 200-300 mg of activated 5Å MS were suspended in toluene (11.0 mL) and the reaction mixture heated to reflux until disappearance of the starting material (TLC Pentane:Ethyl Acetate 4:1). The reaction was quenched with 1 M HCl and water; the aqueous layer was extracted with diethyl ether (2 x 30 mL). The organic layers were collected and washed with NaHCO₃ and brine and then dried over MgSO₄. Filtration and removal of the solvent under reduced pressure afforded the title compound **11** (0.121 g, 0.375 mmol, 19 % yield) that was obtained as a colorless oil used without further purification in the following step.

R_F 0.2 (Pentane:Ethyl Acetate 2:1)

¹H NMR (400 MHz, Chloroform-*d*) δ 7.70 (d, *J* = 8.5 Hz, 1H, *ArH*), 7.48 – 7.40 (m, 2H, *Ph*), 7.39 – 7.28 (m, 3H, *Ph*), 6.95 – 6.85 (m, 2H, *ArH*), 5.55 (s, 1H, CPhCH₂), 5.44 (s, 1H, CPhCH₂), 5.15 – 5.01 (m, 2H, CH₂CPh), 3.89 (s, 3H, OMe), 3.74 (dd, *J* = 8.2, 3.9 Hz, 1H, CH), 3.44 (dd, *J* = 17.3, 3.9 Hz, 1H, CH₂), 3.28 (dd, *J* = 17.3, 8.2 Hz, 1H, CH₂).¹⁶

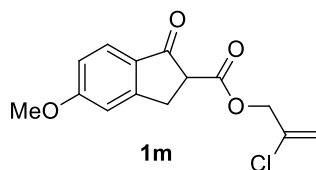
¹³C NMR (101 MHz, Chloroform-*d*) δ 197.4, 169.3, 166.0, 156.7, 142.2, 138.1, 128.6, 128.2, 126.5, 126.2, 116.1, 115.4, 112.7, 109.7, 66.7, 55.9, 53.6, 30.4.

IR ν_{max} 3060 (w), 2941 (w), 2842 (w), 1741 (m), 1705 (s), 1600 (s), 1493 (w), 1307 (w), 1262 (s), 1156 (w), 1091 (m), 1027 (w)

¹⁶ The compound was used in the next step without further purifications, compound **51** was obtained in a 1:0.78 ratio mixture with compound **30**.

HRMS (ESI) calcd for C₂₀H₁₉O₄⁺ [M+H]⁺ 323.1278; found 323.1276.

2-Chloroallyl 5-methoxy-1-oxo-2,3-dihydro-1H-indene-2-carboxylate (1m)



Substrate **1m** was synthesized following a reported procedure,¹⁷ in a 2-neck 50 mL flask compound **22** (0.71 g, 3.0 mmol), DMAP (0.37 g, 3.0 mmol, 1.0 equiv.), 2-chloroprop-2-en-1-ol (0.29 g, 3.2 mmol, 1.05 equiv.) and c.a 200-300 mg of activated 5Å MS were suspended in toluene (11.0 mL) and the reaction mixture heated to reflux till disappearance of the starting material (TLC 9:1, Pentane:Ethyl Acetate). The reaction was quenched with 1 M HCl and water; the aqueous layer was extracted with diethyl ether (2x 30 mL). The organic layers were collected, washed with NaHCO₃, brine, dried over MgSO₄, filtered and concentrated under reduced pressure. The crude is purified by column chromatography: 1:1 DCM:Pentane, 4:1 DCM/Pentane and then 100% DCM. The title compound **1m** (0.49 g, 1.8 mmol, 58% yield) was obtained as yellow oil.

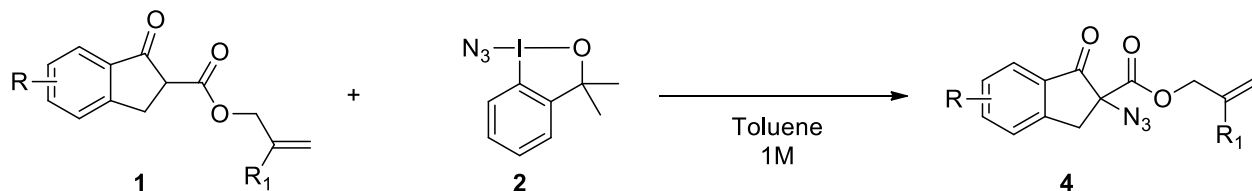
¹H NMR (400 MHz, Chloroform-*d*) δ 7.69 (d, *J* = 9.2 Hz, 1H, Ar*H*), 6.99 – 6.83 (m, 2H, Ar*H*), 5.58 (q, *J* = 1.5 Hz, 1H, CClCH₂), 5.40 (dt, *J* = 1.9, 0.8 Hz, 1H, CClCH₂), 4.86 – 4.63 (m, 2H, CH₂CCl), 3.89 (s, 3H, OMe), 3.77 (dd, *J* = 8.2, 4.0 Hz, 1H, CH), 3.52 (dd, *J* = 17.4, 4.0 Hz, 1H, CH₂), 3.33 (dd, *J* = 17.3, 8.2 Hz, 1H, CH₂).

¹³C NMR (101 MHz, Chloroform-*d*) δ 197.0, 168.5, 166.0, 156.6, 135.1, 128.3, 126.4, 116.1, 114.8, 109.6, 66.4, 55.8, 53.3, 30.2.

IR ν_{max} 2944 (w), 2843 (w), 1746 (m), 1705 (s), 1599 (s), 1491 (w), 1337 (w), 1306 (m), 1259 (s), 1190 (w), 1144 (m), 1105 (m), 1089 (m), 1026 (w), 987 (w).

4. General procedures for the synthesis of α-substituted allyl β-keto esters.

General procedure GP2 for the synthesis of α-azido allyl β-keto esters.



In an open flask allyl β-keto ester **1** in toluene (1 M) is stirred for 1-2 minutes before the addition in one portion of the hypervalent iodine reagent **2** (1.3 equiv.). The reaction was stirred at room temperature till disappearance of the starting material by TLC. Upon completion the reaction was directly purified by flash chromatography in 100% pentane and then following the polarity of the R_F indicated for each compound.

¹⁷ J. Hierold, D. W. Lupton, *Org. Lett.* **2012**, 14, 3412.

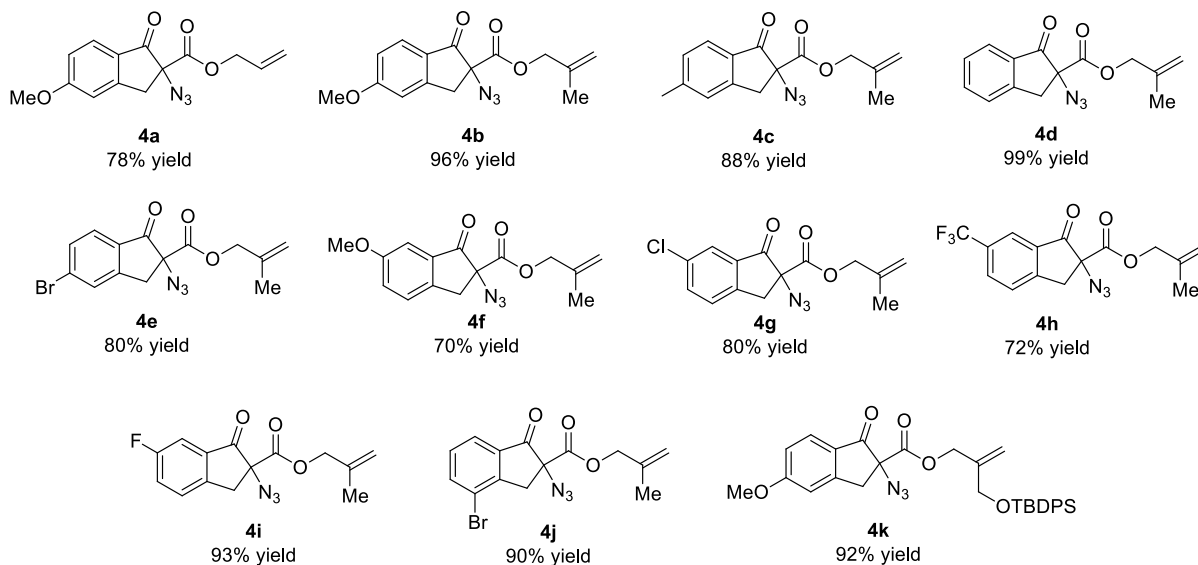
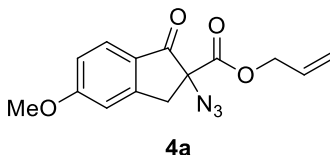


Figure S1. Scope of the α -azidation of β -allyl keto esters with hypervalent iodine reagents.

Allyl 2-azido-5-methoxy-1-oxo-2,3-dihydro-1*H*-indene-2-carboxylate (4a)



Following general procedure GP2, starting from 5-methoxy-1-oxo-2,3-dihydro-1*H*-indene-2-carboxylate (**1a**) (0.52 g, 2.1 mmol), allyl 2-azido-5-methoxy-1-oxo-2,3-dihydro-1*H*-indene-2-carboxylate (**4a**) (0.470 g, 1.65 mmol, 78% yield) was obtained as a brown solid

R_F 0.3 (Pentane:Ethyl Acetate 9:1).

Mp = 55-57°C

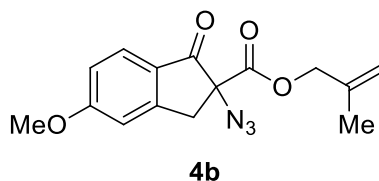
¹H NMR (400 MHz, Chloroform-*d*) δ 7.68 (d, J = 8.6 Hz, 1H, Ar*H*), 6.92 (dd, J = 8.6, 2.3 Hz, 1H, Ar*H*), 6.86 (d, J = 2.4 Hz, 1H, Ar*H*), 5.80 (m, J = 17.2, 10.5, 5.6 Hz, 1H, CHCH₂), 5.28 – 5.09 (m, 2H, CHCH₂), 4.72 – 4.57 (m, 2H, CH₂CH), 3.86 (s, 3H, OMe), 3.59 (d, J = 17.4 Hz, 1H, CH₂), 2.93 (dd, J = 17.4, 0.9 Hz, 1H, CH₂).

¹³C NMR (101 MHz, Chloroform-*d*) δ 195.2, 168.4, 166.8, 155.3, 130.9, 127.3, 125.9, 119.0, 116.7, 109.6, 70.5, 66.9, 55.9, 38.4.

IR ν_{max} 3080 (w), 2944 (w), 2844 (w), 2108 (s), 1747 (m), 1711 (s), 1599 (s), 1307 (w), 1264 (s), 1231 (s), 1184 (m), 1152 (w), 1091 (m), 1045 (m), 1026 (m), 929 (w).

HRMS (ESI) calcd for C₁₄H₁₃N₃NaO₄⁺ [M+Na]⁺ 310.0798; found 310.0795.

2-Methylallyl 2-azido-5-methoxy-1-oxo-2,3-dihydro-1H-indene-2-carboxylate (4b)



Following general procedure **GP2**, starting from 2-methylallyl 5-methoxy-1-oxo-2,3-dihydro-1H-indene-2-carboxylate (**1b**) (1.0 g, 3.9 mmol, 2-methylallyl 2-azido-5-methoxy-1-oxo-2,3-dihydro-1H-indene-2-carboxylate (**4b**) (1.1 g, 3.8 mmol, 96% yield) was obtained as a yellow solid.

R_F 0.35 (Pentane:Ethyl Acetate 4:1).

Mp: 41-44°C.

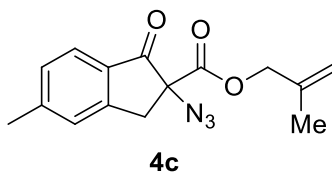
¹H NMR (400 MHz, Chloroform-*d*) δ 7.76 (d, *J* = 8.6 Hz, 1H, Ar*H*), 6.97 (dd, *J* = 8.6, 2.2 Hz, 1H, Ar*H*), 6.88 (d, *J* = 2.3 Hz, 1H, Ar*H*), 4.91 (s, 2H, CCH₂), 4.63 (s, 2H, CH₂CMe), 3.91 (s, 3H, OMe), 3.64 (d, *J* = 17.3 Hz, 1H, CH₂), 2.99 (d, *J* = 17.3 Hz, 1H, CH₂), 1.69 (d, *J* = 1.2 Hz, 3H, CH₃).

¹³C NMR (101 MHz, Chloroform-*d*) δ 195.2, 168.5, 166.7, 155.2, 138.8, 127.4, 126.1, 116.6, 113.9, 109.6, 70.6, 69.7, 55.9, 38.5, 19.3.

IR ν_{max} 2108 (m), 1748 (m), 1710 (m), 1599 (s), 1493 (w), 1448 (w), 1342 (w), 1306 (w), 1265 (s), 1230 (m), 1184 (m), 1148 (w), 1092 (w), 1024 (w), 982 (w), 909 (w), 850 (w), 737 (w).

HRMS (ESI) calcd for C₁₅H₁₅N₃NaO₄⁺ [M+Na]⁺ 324.0955; found 324.0961.

2-Methylallyl 2-azido-5-methyl-1-oxo-2,3-dihydro-1H-indene-2-carboxylate (4c)



Following general procedure **GP2**, starting from 2-methylallyl 5-methyl-1-oxo-2,3-dihydro-1H-indene-2-carboxylate (**1c**) (0.158 g, 0.647 mmol), 2-methylallyl 2-azido-5-methyl-1-oxo-2,3-dihydro-1H-indene-2-carboxylate (**4c**) (0.162 g, 0.568 mmol, 88% yield) was obtained as a yellow solid.

R_F 0.52 (Pentane:Ethyl Acetate 4:1).

Mp: 36-39°C.

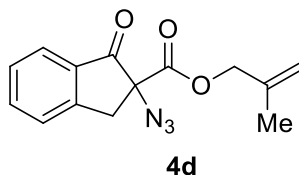
¹H NMR (400 MHz, Chloroform-*d*) δ 7.24 – 7.20 (m, 1H, Ar*H*), 6.79 – 6.72 (m, 2H, Ar*H*), 4.40 (s, 2H, CMeCH₂), 4.12 (s, 2H, CH₂CMe), 3.15 (d, *J* = 17.3 Hz, 1H, CH₂), 2.50 (d, *J* = 17.3 Hz, 1H, CH₂), 1.97 (s, 3H, ArCH₃), 1.18 (s, 3H, CH₃).

¹³C NMR (101 MHz, Chloroform-*d*) δ 196.7, 168.3, 152.5, 148.2, 138.8, 130.8, 129.8, 126.8, 125.4, 113.9, 70.5, 69.7, 38.4, 22.3, 19.3.

IR ν_{max} 2974 (w), 2973 (w), 2938 (w), 2938 (w), 2109 (s), 2108 (s), 1748 (s), 1716 (s), 1609 (m), 1270 (s), 1225 (s), 1181 (s), 1045 (m), 908 (m), 754 (m), 744 (m), 737 (m).

HRMS (APPI) calcd for C₁₅H₁₆NO₃⁺ [M-N₂]⁺ 258.1125; found 258.1126

2-Methylallyl 2-azido-1-oxo-2,3-dihydro-1*H*-indene-2-carboxylate (4d)



Following general procedure **GP2**, starting from 2-methylallyl 1-oxo-2,3-dihydro-1*H*-indene-2-carboxylate (**1d**) (0.25 g, 1.1 mmol), 2-methylallyl 2-azido-1-oxo-2,3-dihydro-1*H*-indene-2-carboxylate (**4d**) (0.10 g, 1.1 mmol, >99% yield) was obtained as a yellow oil

R_F 0.33 (Dichloromethane:Pentane 5:1).

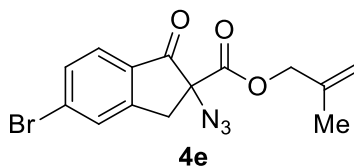
¹H NMR (400 MHz, Chloroform-*d*) δ 7.84 (dt, J = 7.7, 1.0 Hz, 1H, Ar*H*), 7.68 (dd, J = 7.6, 1.2 Hz, 1H, Ar*H*), 7.53 – 7.40 (m, 2H, Ar*H*), 4.93 – 4.84 (m, 2H, C CH₂), 4.62 (s, 2H, CH₂C), 3.70 (d, J = 17.3 Hz, 1H, CH₂), 3.06 (d, J = 17.3 Hz, 1H, CH₂), 1.67 (s, 3H, CH₃).

¹³C NMR (101 MHz, Chloroform-*d*) δ 197.4, 168.2, 152.0, 138.7, 136.5, 133.1, 128.5, 126.4, 125.6, 114.0, 70.3, 69.8, 38.6, 19.3.

IR ν_{max} 3057 (w), 2985 (w), 2114 (w), 1750 (w), 1723 (w), 1266 (m), 1228 (w), 1185 (w), 738 (s).

HRMS (ESI) calcd for C₁₄H₁₄NO₃⁺ [M-N₂+H]⁺ 244.0968; found 244.0957.

2-Methylallyl 2-azido-5-bromo-1-oxo-2,3-dihydro-1*H*-indene-2-carboxylate (4e)



Following general procedure **GP2**, starting from 2-methylallyl 5-bromo-1-oxo-2,3-dihydro-1*H*-indene-2-carboxylate (**1e**) (0.11 g, 0.36 mmol), 2-methylallyl 2-azido-5-bromo-1-oxo-2,3-dihydro-1*H*-indene-2-carboxylate (**4e**) (0.10 g, 0.29 mmol, 80 % yield) was obtained as a yellow solid.

R_F 0.52 (Pentane:Ethyl Acetate 9:1).

Mp: 71-73°C.

¹H NMR (400 MHz, Chloroform-*d*) δ 7.69 (d, J = 8.2 Hz, 1H, Ar*H*), 7.66 (d, J = 1.3 Hz, 1H, Ar*H*), 7.60 (dd, J = 8.2, 1.5 Hz, 1H, Ar*H*), 4.92 (s, 1H, CCH₂), 4.90 (s, 1H, CCH₂), 4.63 (s, 2H,

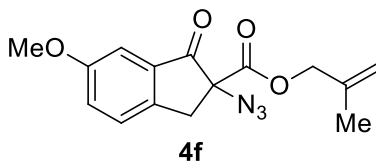
CH_2CMe), 3.67 (d, $J = 17.5$ Hz, 1H, CH_2), 3.03 (d, $J = 17.5$ Hz, 1H, CH_2), 1.69 (t, $J = 1.1$ Hz, 3H, CH_3).

^{13}C NMR (101 MHz, Chloroform- d) δ 196.3, 167.8, 153.4, 138.6, 132.2, 132.2, 131.9, 129.8, 126.7, 114.2, 70.2, 70.0, 38.2, 19.3.

IR ν_{max} 2946 (w), 2919 (w), 2114 (s), 1752 (s), 1726 (s), 1681 (w), 1597 (m), 1264 (s), 1230 (s), 1183 (m), 911 (m), 910 (m).

HRMS (APPI) calcd for $\text{C}_{14}\text{H}_{13}^{79}\text{BrN}_3\text{O}_3^+$ $[\text{M}+\text{H}]^+$ 349.0062; found $[\text{M}-\text{N}_2+\text{H}]^+$ 322.0072.

2-Methylallyl 2-azido-6-methoxy-1-oxo-2,3-dihydro-1H-indene-2-carboxylate (4f)



Following general procedure **GP2**, starting from 2-methylallyl 6-methoxy-1-oxo-2,3-dihydro-1H-indene-2-carboxylate (**1f**) (0.15 g, 0.58 mmol), 2-methylallyl 2-azido-6-methoxy-1-oxo-2,3-dihydro-1H-indene-2-carboxylate (**4f**) (0.12 g, 0.41 mmol, 70% yield) was obtained as yellow solid.

R_F 0.85 (Pentane:Ethyl Acetate 4:1).

Mp: 50-53°C

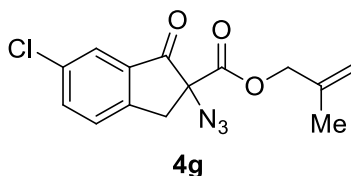
^1H NMR (400 MHz, Chloroform- d) 7.36 (d, $J = 8.4$ Hz, 1H, ArH), 7.27 (dd, $J = 8.4, 2.6$ Hz, 1H, ArH), 7.23 (d, $J = 2.5$ Hz, 1H, ArH), 4.90 (m, 2H, CMeCH_2), 4.62 (s, 2H, CH_2CMe), 3.85 (s, 3H, OMe), 3.62 (d, $J = 17.0$ Hz, 1H, CH_2), 2.98 (d, $J = 16.9$ Hz, 1H, CH_2), 1.68 (t, $J = 1.2$ Hz, 3H, CH_3).

^{13}C NMR (101 MHz, Chloroform- d) δ 197.3, 168.2, 160.1, 145.0, 138.7, 134.2, 127.1, 126.0, 113.9, 106.4, 71.0, 69.7, 55.7, 38.0, 19.3.

IR ν_{max} 3081 (w), 2943 (w), 2841 (w), 2112 (s), 1748 (s), 1718 (s), 1494 (m), 1302 (m), 1275 (s), 1228 (s), 1180 (s), 1029 (m).

HRMS (APPI) calcd for $\text{C}_{15}\text{H}_{16}\text{N}_3\text{O}_4^+$ $[\text{M}+\text{H}]^+$ 302.1135; found 302.1136.

2-Methylallyl 2-azido-6-chloro-1-oxo-2,3-dihydro-1H-indene-2-carboxylate (4g)



Following general procedure **GP2**, starting from 2-methylallyl 6-chloro-1-oxo-2,3-dihydro-1H-indene-2-carboxylate (**1g**) (0.167 g, 0.631 mmol), 2-methylallyl 2-azido-6-chloro-1-oxo-2,3-

dihydro-1*H*-indene-2-carboxylate (**4g**) (0.154 g, 0.504 mmol, 80% yield) was obtained as a dark brown oil.

R_F 0.4 (Dichloromethane:Pentane 1:1).

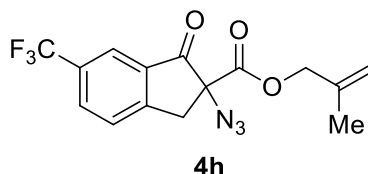
¹H NMR (400 MHz, Chloroform-*d*) 7.79 (d, *J* = 2.0 Hz, 1H, Ar*H*), 7.64 (dd, *J* = 8.2, 2.1 Hz, 1H, Ar*H*), 7.42 (dd, *J* = 8.2, 0.8 Hz, 1H, Ar*H*), 4.92 (m, 1H, CMeCH₂), 4.63 (s, 2H, CH₂CMe), 3.66 (d, *J* = 17.6 Hz, 1H, CH₂), 3.02 (dd, *J* = 17.4, 0.9 Hz, 1H, CH₂), 1.78 – 1.60 (m, 3H, CH₃).

¹³C NMR (101 MHz, Chloroform-*d*) δ 196.3, 167.8, 150.1, 138.6, 136.5, 134.9, 134.6, 127.6, 125.2, 114.2, 70.7, 70.0, 38.2, 19.3.

IR ν_{max} 3086 (w), 2954 (w), 2941 (w), 2114 (s), 1752 (s), 1724 (s), 1469 (w), 1429 (m), 1252 (s), 1227 (s), 1197 (s), 1185 (s), 1110 (w), 1047 (m), 910 (m), 826 (w), 714 (m).

HRMS (ESI) calcd for C₁₄H₁₃ClNO₃⁺ [M+H]⁺ 278.0578; found 278.0581.

2-Methylallyl 2-azido-1-oxo-6-(trifluoromethyl)-2,3-dihydro-1*H*-indene-2-carboxylate (4h)



Following general procedure **GP2**, starting from 2-methylallyl 1-oxo-6-(trifluoromethyl)-2,3-dihydro-1*H*-indene-2-carboxylate (**1h**) (0.25 g, 0.83 mmol), 2-methylallyl 2-azido-1-oxo-6-(trifluoromethyl)-2,3-dihydro-1*H*-indene-2-carboxylate (**4h**) (0.20 g, 0.60 mmol, 72% yield) was obtained as dark brown oil.

R_F 0.35 (Pentane:Ethyl Acetate 9:1).

¹H NMR (400 MHz, Chloroform-*d*) δ 8.08 (s, 1H, Ar*H*), 7.93 (dd, *J* = 8.1, 1.7 Hz, 1H, Ar*H*), 7.64 (d, *J* = 8.1 Hz, 1H, Ar*H*), 4.93 (t, *J* = 1.4 Hz, 1H, CMeCH₂), 4.90 (q, *J* = 1.2 Hz, 1H, CMeCH₂), 4.63 (s, 2H, CH₂CMe), 3.76 (d, *J* = 17.8 Hz, 1H, CH₂), 3.12 (d, *J* = 17.7 Hz, 1H, CH₂), 1.67 (t, *J* = 1.1 Hz, 3H, CH₃).

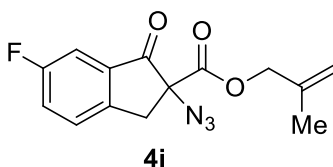
¹³C NMR (101 MHz, CDCl₃) δ 196.4, 167.6, 155.1, 138.5, 133.5, 132.8 (d, *J* = 3.5 Hz), 131.4 (q, *J* = 33.5 Hz), 127.3, 123.5 (q, *J* = 272.9 Hz), 122.8 (q, *J* = 4.0 Hz), 114.3, 70.4, 70.1, 38.6, 19.3.

¹⁹F NMR (376 MHz, CDCl₃) δ -62.7.

IR ν_{max} 2982 (w), 2945 (w), 2116 (m), 1752 (m), 1729 (m), 1626 (w), 1332 (s), 1254 (s), 1228 (m), 1173 (s), 1131 (s), 1054 (m), 912 (m).

HRMS (ESI) calcd for C₁₅H₁₂F₃N₃NaO₃⁺ [M+Na]⁺ 362.0728; found 362.0731.

2-Methylallyl 2-azido-6-fluoro-1-oxo-2,3-dihydro-1H-indene-2-carboxylate (4i)



Following general procedure **GP2**, starting from 2-methylallyl 6-fluoro-1-oxo-2,3-dihydro-1H-indene-2-carboxylate (**1i**) (0.20 g, 0.80 mmol), 2-methylallyl 2-azido-6-fluoro-1-oxo-2,3-dihydro-1H-indene-2-carboxylate (**4i**) (0.21 g, 0.75 mmol, 93% yield) was obtained as a yellow oil.

R_F 0.3 (Dichloromethane:Pentane 5:1).

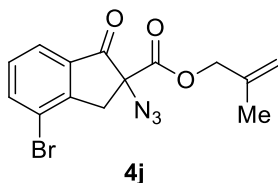
¹H NMR (400 MHz, Chloroform-*d*) δ 7.52 – 7.35 (m, 3H, ArH), 4.91 (m, 1H, CCH₂), 4.89 (m, 1H, CCH₂), 4.63 (s, 2H, CH₂CMe), 3.66 (dt, *J* = 17.1, 1.1 Hz, 1H, CH₂), 3.02 (dt, *J* = 17.2, 1.3 Hz, 1H, CH₂), 1.68 (t, *J* = 1.1 Hz, 3H, CH₃).

¹³C NMR (101 MHz, Chloroform-*d*) δ 196.6, 167.8, 162.7 (d, *J* = 250.1 Hz), 147.5 (d, *J* = 2.4 Hz), 138.6, 134.8 (d, *J* = 7.7 Hz), 127.9 (d, *J* = 8.0 Hz), 124.3 (d, *J* = 23.7 Hz), 114.1, 111.34 (d, *J* = 22.4 Hz), 71.0, 70.0, 38.1, 19.3.

IR ν_{max} 3081 (w), 2982 (w), 2945 (w), 2114 (s), 1750 (s), 1726 (s), 1490 (m), 1440 (w), 1331 (m), 1259 (s), 1226 (s), 1180 (s), 1132 (s), 1051 (m), 912 (m).

HRMS (ESI) calcd for C₁₄H₁₃FN₃O₃⁺ [M+H]⁺ 290.0935; found 290.1006.

2-Methylallyl 2-azido-4-bromo-1-oxo-2,3-dihydro-1H-indene-2-carboxylate (4j)



Following general procedure **GP2**, starting from 2-methylallyl 4-bromo-1-oxo-2,3-dihydro-1H-indene-2-carboxylate (**1j**) (0.11 g, 0.37 mmol), 2-methylallyl 2-azido-4-bromo-1-oxo-2,3-dihydro-1H-indene-2-carboxylate (**4j**) (0.11 g, 0.33 mmol, 90% yield) was obtained as a colorless oil.

R_F 0.32 (Pentane:Ethyl Acetate 9:1).

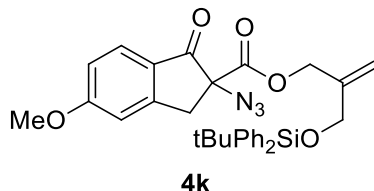
¹H NMR (400 MHz, Chloroform-*d*) δ 7.84 (dd, *J* = 7.8, 1.0 Hz, 1H, ArH), 7.78 (dd, *J* = 7.7, 0.9 Hz, 1H, ArH), 7.36 (t, *J* = 7.7 Hz, 1H, ArH), 4.92 (s, 1H, CMeCH₂), 4.90 (s, 1H, CMeCH₂), 4.64 (s, 2H, CH₂CMe), 3.62 (d, *J* = 17.8 Hz, 1H, CH₂), 2.98 (d, *J* = 17.8 Hz, 1H, CH₂), 1.68 (s, 3H, CH₃).

¹³C NMR (101 MHz, Chloroform-*d*) δ 196.8, 167.7, 151.7, 139.2, 138.6, 135.0, 130.2, 124.4, 121.7, 114.2, 70.1, 70.0, 39.7, 19.3.

IR ν_{\max} 2116 (s), 1754 (s), 1727 (s), 1261 (s), 1227 (s), 1184 (w), 1111 (w), 1045 (w), 918 (w), 776 (w), 716 (w).

HRMS (APPI) calcd for $C_{14}H_{12}BrN_3NaO_3^+ [M+Na]^+$ 371.9960; found 371.9962.

2-(((tert-butyldiphenylsilyl)oxy)methyl)allyl 2-azido-5-methoxy-1-oxo-2,3-dihydro-1H-indene-2-carboxylate (4k)



Following general procedure **GP2**, starting from 2-(((tert-butyldiphenylsilyl)oxy)methyl)allyl 5-methoxy-1-oxo-2,3-dihydro-1H-indene-2-carboxylate (**1k**) (0.17 g, 0.34 mmol), 2-(((tert-butyldiphenylsilyl)oxy)methyl)allyl 2-azido-5-methoxy-1-oxo-2,3-dihydro-1H-indene-2-carboxylate (**4k**) (0.17 g, 0.31 mmol, 92% yield) was obtained as a yellow oil.

R_F 0.3 (Pentane: Ethyl Acetate 9:1).

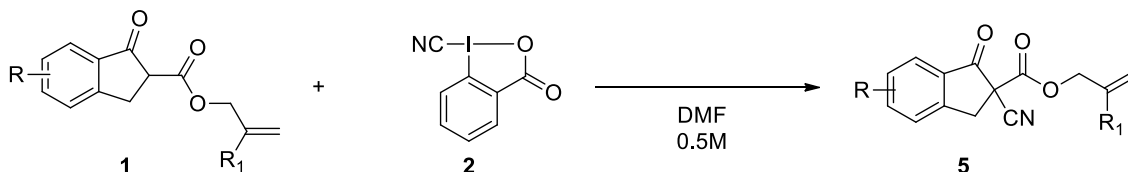
¹H NMR (400 MHz, Chloroform-*d*) δ 7.70 (d, J = 8.6 Hz, 1H, ArH), 7.65 – 7.59 (m, 4H, Ph), 7.47 – 7.33 (m, 6H, Ph), 6.93 (dd, J = 8.6, 2.2 Hz, 1H, ArH), 6.81 – 6.77 (m, 1H, ArH), 5.27 – 5.24 (m, 1H, CCH₂), 5.09 (q, J = 1.3 Hz, 1H, CCH₂), 4.79 (dd, J = 13.0, 0.7 Hz, 1H, CH₂CCH₂), 4.71 (dd, J = 13.1, 0.6 Hz, 1H, CH₂CCH₂), 4.17 – 4.03 (m, 2H, CCH₂OTBDPS), 3.88 (s, 3H, OMe), 3.53 (dd, J = 17.4, 0.9 Hz, 1H, CH₂), 2.92 (d, J = 17.6 Hz, 1H, CH₂), 1.03 (s, 9H, *t*Bu).

¹³C NMR (101 MHz, Chloroform-*d*) δ 195.1, 168.3, 166.6, 155.1, 141.6, 135.5, 133.3, 133.2, 129.8, 127.7, 127.4, 126.0, 116.5, 113.6, 109.5, 70.6, 66.6, 64.4, 55.9, 38.5, 26.8, 19.3.¹⁸

IR ν_{\max} 3070 (w), 2960 (w), 2936 (w), 2860 (w), 2110 (m), 1749 (w), 1713 (m), 1601 (m), 1266 (s), 1232 (w), 1181 (w), 1109 (m), 1093 (m), 910 (s), 704 (s).

HRMS (ESI) calcd for $C_{31}H_{34}NO_5Si^+ [M+H-N_2]^+$ 528.2201; found 528.2178

General procedure GP3 for the synthesis of α -cyano allyl β -keto esters.



Following a reported procedure **GP3**, in an open flask allyl β -keto ester **1** is stirred in DMF (0.5 M) for 1-2 minutes before the addition in one portion of the hypervalent iodine reagent **7** (1.1 equiv.) The reaction is stirred at room temperature till disappearance of the starting material by TLC. Upon completion the reaction is directly purified by flash chromatography in 100% pentane and then following the solvent polarity indicated for the R_F of each compound.

¹⁸ 3 C of the phenyls group of the TBDPS are not resolved.

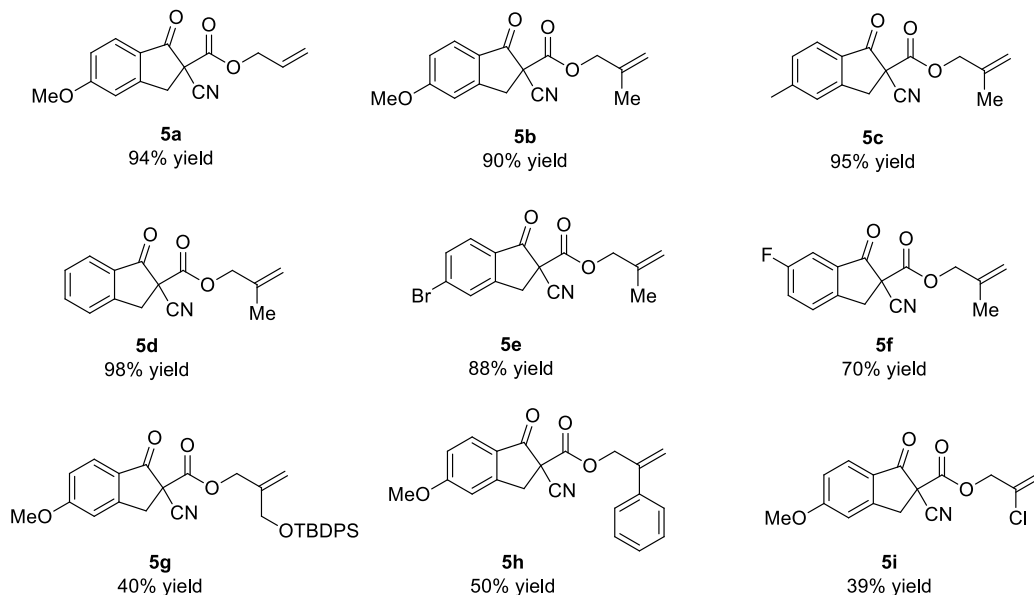
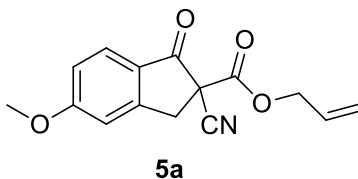


Figure S2. Scope of the α -cyanation of β -allyl keto esters with hypervalent iodine reagents.

Allyl 2-cyano-5-methoxy-1-oxo-2,3-dihydro-1*H*-indene-2-carboxylate (**5a**)



Following general procedure **GP3**, starting from allyl 5-methoxy-1-oxo-2,3-dihydro-1*H*-indene-2-carboxylate (**1a**) (0.500 g, 2.03 mmol), allyl 2-cyano-5-methoxy-1-oxo-2,3-dihydro-1*H*-indene-2-carboxylate (**5a**) (0.518 g, 1.91 mmol, 94% yield) was obtained as a light yellow oil.

R_F 0.30 (Pentane:Ethyl Acetate 4:1).

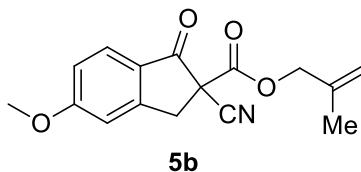
¹H NMR (400 MHz, Chloroform-*d*) δ 7.78 (d, J = 8.6 Hz, 1H, Ar*H*), 7.00 (dd, J = 8.6, 2.2 Hz, 1H, Ar*H*), 6.94 (d, J = 2.2 Hz, 1H, Ar*H*), 5.92 (ddt, J = 17.0, 10.5, 5.6 Hz, 1H, CHCH₂), 5.40 (dd, J = 17.0, 1.2 Hz, 1H, CCH₂), 5.30 (dd, J = 10.5, 1.2 Hz, 1H, CCH₂), 4.75 (dd, J = 5.6, 1.2 Hz, 2H, CH₂CH), 3.93 (s, 3H, OMe), 3.89 (d, J = 17.3 Hz, 1H, CH₂), 3.63 (d, J = 17.3 Hz, 1H, CH₂).

¹³C NMR (101.00 MHz, Chloroform-*d*) δ 188.5, 167.2, 164.2, 154.9, 130.5, 128.2, 125.1, 119.8, 117.4, 116.5, 109.7, 68.2, 56.1, 54.7, 37.6.

IR ν_{max} 3017 (w), 2949 (w), 2844 (w), 2249 (w), 1750 (m), 1722 (s), 1601 (s), 1494 (w), 1311 (m), 1269 (s), 1093 (m).

HRMS (ESI) calcd for C₁₅H₁₄NO₄⁺ [M+H]⁺ 272.0917; found 272.0927.

2-Methylallyl 2-cyano-5-methoxy-1-oxo-2,3-dihydro-1*H*-indene-2-carboxylate (**5b**)



Following general procedure **GP3**, starting from 2-methylallyl 5-methoxy-1-oxo-2,3-dihydro-1*H*-indene-2-carboxylate (**1b**) (1.0 g, 3.8 mmol), 2-methylallyl 2-cyano-5-methoxy-1-oxo-2,3-dihydro-1*H*-indene-2-carboxylate (**5b**) (0.981 g, 3.44 mmol, 90% yield) was obtained as a yellow resin.

R_F 0.25 (Pentane:Ethyl Acetate 4:1).

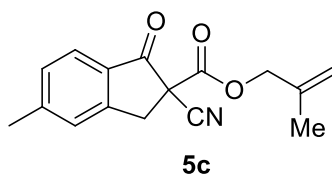
¹H NMR (400 MHz, Chloroform-*d*) δ 7.70 (d, J = 8.6 Hz, 1H, Ar*H*), 6.93 (dd, J = 8.6, 1.9 Hz, 1H, Ar*H*), 6.89 – 6.85 (m, 1H, Ar*H*), 4.98 – 4.95 (s, 1H, CCH₂), 4.92 – 4.89 (s, 1H, CCH₂), 4.64 – 4.54 (m, 2H, CH₂CMe), 3.86 (s, 3H, OMe), 3.83 (d, J = 17.2 Hz, 1H, CH₂), 3.56 (d, J = 17.2 Hz, 1H, CH₂), 1.70 (s, 3H, CH₃).

¹³C NMR (101.00 MHz, Chloroform-*d*) δ 188.5, 167.2, 164.2, 154.9, 138.5, 128.2, 125.1, 117.4, 116.2, 114.5, 109.6, 70.9, 56.2, 54.8, 37.5, 19.4.

IR ν_{max} 2983 (w), 2946 (w), 2844 (w), 2250 (w), 1751 (m), 1725 (s), 1600 (s), 1451 (w), 1268 (s), 1209 (m), 1093 (m).

HRMS (ESI) calcd for C₁₆H₁₆NO₄⁺ [M+H]⁺ 286.1074; found 286.1085.

2-Methylallyl 2-cyano-5-methyl-1-oxo-2,3-dihydro-1*H*-indene-2-carboxylate (**5c**)



Following general procedure **GP3**, starting from 2-methylallyl 5-methyl-1-oxo-2,3-dihydro-1*H*-indene-2-carboxylate (**1c**) (0.195 g, 0.800 mmol), 2-methylallyl 2-cyano-5-methyl-1-oxo-2,3-dihydro-1*H*-indene-2-carboxylate (**5c**) (0.204 g, 0.758 mmol, 95% yield) was obtained as a yellow oil.

R_F 0.3 (Pentane:Ethyl Acetate 4:1).

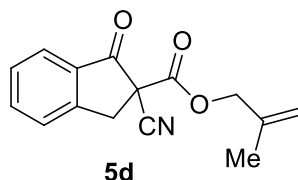
¹H NMR (400 MHz, Chloroform-*d*) δ 7.74 (d, J = 8.0 Hz, 1H, Ar*H*), 7.34 (s, 1H, Ar*H*), 7.30 (d, J = 8.0 Hz, 1H, Ar*H*), 5.03 (s, 1H, CCH₂), 4.97 (s, 1H, CCH₂), 4.66 (m, 2H, CH₂CMe), 3.90 (d, J = 17.2 Hz, 1H, CH₂), 3.64 (d, J = 17.2 Hz, 1H, CH₂), 2.49 (s, 3H, CH₃), 1.77 (s, 3H, CH₃).

¹³C NMR (101.00 MHz, Chloroform-*d*) δ 190.0, 164.1, 152.2, 149.1, 138.5, 130.5, 129.9, 126.9, 126.3, 116.0, 114.5, 70.9, 54.7, 37.5, 22.5, 19.4.

IR ν_{max} 2983 (w), 2944 (w), 2865 (w), 2248 (w), 1731 (s), 1609 (m), 1452 (w), 1266 (m), 1207 (m), 905 (w).

HRMS (ESI) calcd for $\text{C}_{16}\text{H}_{15}\text{NNaO}_3^+$ $[\text{M}+\text{Na}]^+$ 292.0944; found 292.0951.

2-Methylallyl 2-cyano-1-oxo-2,3-dihydro-1*H*-indene-2-carboxylate (**5d**)



Following general procedure **GP3**, starting from 2-methylallyl 1-oxo-2,3-dihydro-1*H*-indene-2-carboxylate (**1d**) (0.184 g, 0.800 mmol), 2-methylallyl 2-cyano-1-oxo-2,3-dihydro-1*H*-indene-2-carboxylate (**5d**) (0.201 g, 0.787 mmol, 98% yield) was obtained as a pale yellow oil.

R_F 0.2 (Pentane:Ethyl Acetate 4:1).

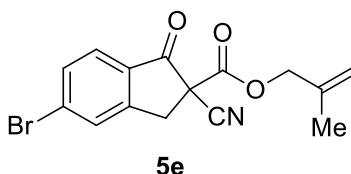
¹H NMR (400 MHz, Chloroform-*d*) δ 7.86 (d, $J = 7.9$ Hz, 1H, Ar*H*), 7.74 (td, $J = 7.5, 1.2$ Hz, 1H, Ar*H*), 7.58 – 7.47 (m, 2H, Ar*H*), 5.02 (s, 1H, CCH₂), 4.98 (s, 1H, CCH₂), 4.73 – 4.62 (m, 2H, CH₂CMe), 3.96 (d, $J = 17.2$ Hz, 1H, CH₂), 3.71 (d, $J = 17.3$ Hz, 1H, CH₂), 1.76 (s, 3H, CH₃).

¹³C NMR (101.00 MHz, Chloroform-*d*) δ 190.7, 163.9, 151.6, 138.4, 137.2, 132.3, 129.2, 126.6, 126.5, 115.8, 114.6, 71.0, 54.5, 37.7, 19.4.

IR ν_{max} 3082 (w), 2983 (w), 2945 (w), 2250 (w), 1733 (s), 1603 (w), 1466 (w), 1436 (w), 1263 (m), 1205 (m), 909 (m).

HRMS (ESI) HRMS (ESI) calcd for $\text{C}_{15}\text{H}_{13}\text{NNaO}_3^+$ $[\text{M}+\text{Na}]^+$ 278.0788; found 278.0791.

2-Methylallyl 5-bromo-2-cyano-1-oxo-2,3-dihydro-1*H*-indene-2-carboxylate (**5e**)



Following general procedure **GP3**, starting from 2-methylallyl 5-bromo-1-oxo-2,3-dihydro-1*H*-indene-2-carboxylate (**1e**) (0.200 g, 0.647 mmol), 2-methylallyl 5-bromo-2-cyano-1-oxo-2,3-dihydro-1*H*-indene-2-carboxylate (**5e**) (0.190 g, 0.569 mmol, 88% yield) was obtained as an orange oil.

R_F 0.7 (Pentane:Ethyl Acetate 9:1).

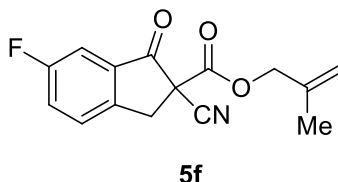
¹H NMR (400 MHz, Chloroform-*d*) δ 7.76 – 7.68 (m, 2H, ArH), 7.67 – 7.62 (m, 1H, ArH), 5.03 (s, 1H, CCH₂), 4.99 (s, 1H, CCH₂), 4.66 (s, 2H, CH₂CMe), 3.94 (d, *J* = 17.4 Hz, 1H, CH₂), 3.68 (d, *J* = 17.5 Hz, 1H, CH₂), 1.77 (s, 3H, CH₃).

¹³C NMR (101.00 MHz, Chloroform-*d*) δ 189.5, 163.5, 152.9, 138.3, 132.9, 131.1, 130.0, 127.4, 115.4, 114.7, 71.2, 54.5, 37.2, 19.4.

IR ν_{max} 3088 (w), 2982 (w), 2943 (w), 2251 (w), 1738 (s), 1595 (m), 1424 (w), 1255 (m), 1060 (w), 909 (m).

HRMS (ESI) calcd for C₁₅H₁₃⁷⁹BrNO₃⁺ [M+H]⁺ 334.0073; found 334.0087.

2-Methylallyl 2-cyano-6-fluoro-1-oxo-2,3-dihydro-1*H*-indene-2-carboxylate (**5f**)



Following general procedure **GP3**, starting from 2-methylallyl 6-fluoro-1-oxo-2,3-dihydro-1*H*-indene-2-carboxylate (**1i**) (0.199 g, 0.800 mmol), 2-methylallyl 2-cyano-6-fluoro-1-oxo-2,3-dihydro-1*H*-indene-2-carboxylate (**5f**) (0.153 g, 0.560 mmol, 70% yield) was obtained as a yellow oil.

R_F 0.7 (Pentane:Ethyl Acetate 4:1).

¹H NMR (400 MHz, Chloroform-*d*) δ 7.54 (m, 1H, ArH), 7.46 (m, 2H, ArH), 4.99 (s, 1H, CCH₂), 4.96 (s, 1H, CCH₂), 4.64 (s, 2H, CH₂CMe), 3.91 (d, *J* = 17.1, 1H, CH₂), 3.67 (d, *J* = 17.1, 1H, CH₂), 1.74 (s, 3H, CH₃).

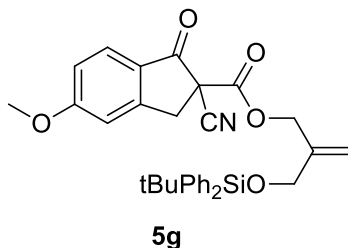
¹³C NMR (101.00 MHz, Chloroform-*d*) δ 189.9, 163.4, 162.9 (d, *J* = 251.2 Hz), 147.2 (d, *J* = 1.9 Hz), 138.2, 133.9 (d, *J* = 8.1 Hz), 128.2 (d, *J* = 8.1 Hz), 125.0 (d, *J* = 23.9 Hz), 115.3, 114.5, 111.9 (d, *J* = 22.8 Hz), 70.9, 55.2, 37.0, 19.2.

IR ν_{max} 3089 (w), 2942 (w), 2869 (w), 2251 (w), 1737 (s), 1600 (w), 1491 (m), 1440 (m), 1298 (m), 1267 (s), 1205 (m).

HRMS (ESI) calcd for C₁₅H₁₂FNNaO₃⁺ [M+Na]⁺ 296.0693; found 296.0696.

2-(((*Tert*-butyldiphenylsilyl)oxy)methyl)allyl
indene-2-carboxylate (**5g**)

2-cyano-5-methoxy-1-oxo-2,3-dihydro-1*H*-



Following general procedure **GP3**, starting from 2-(((*tert*-butyldiphenylsilyl)oxy)methyl)allyl 5-methoxy-1-oxo-2,3-dihydro-1*H*-indene-2-carboxylate (**1k**) (0.412 g, 0.800 mmol), 2-(((*Tert*-butyldiphenylsilyl)oxy)methyl)allyl 2-cyano-5-methoxy-1-oxo-2,3-dihydro-1*H*-indene-2-carboxylate (**5g**) (0.17 g, 0.32 mmol, 40% yield) was obtained as a yellow oil.

R_F 0.5 (Pentane:Ethyl Acetate 4:1).

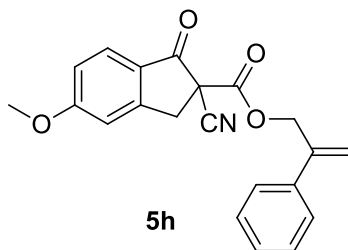
¹H NMR (400 MHz, Chloroform-*d*) δ 7.73 (d, J = 8.6 Hz, 1H, Ar*H*), 7.68 – 7.62 (m, 4H, Ar*H*), 7.40 (m, 6H, Ar*H*), 6.98 (dd, J = 8.6, 2.1 Hz, 1H, Ar*H*), 6.89 (m, 1H, Ar*H*), 5.28 (s, 1H, CCH₂), 5.21 (s, 1H, CCH₂), 4.80 (m, 2H, CH₂CCH₂), 4.19 (m, 2H, CH₂CCH₂), 3.92 (s, 3H, OMe), 3.82 (d, J = 17.3 Hz, 1H, CH₂), 3.58 (d, J = 17.3 Hz, 1H, CH₂), 1.05 (s, 9H, SiC(CH₃)₃).

¹³C NMR (101.00 MHz, Chloroform-*d*) δ 188.4, 167.2, 164.2, 154.8, 141.4, 135.6, 133.4, 129.9, 127.9, 125.1, 117.4, 116.1, 114.1, 109.7, 67.6, 64.6, 56.2, 54.8, 37.5, 26.9, 19.4.

IR ν_{max} 3726 (w), 3708 (w), 3626 (w), 2933 (w), 2857 (w), 2361 (w), 2297 (w), 1752 (m), 1728 (s), 1600 (s), 1429 (w), 1268 (s), 1114 (m).

HRMS (ESI) calcd for C₃₂H₃₃NNaO₅Si⁺ [M+Na]⁺ 562.2020; found 562.2018.

2-Phenylallyl 2-cyano-5-methoxy-1-oxo-2,3-dihydro-1*H*-indene-2-carboxylate (**5h**)



Following general procedure **GP3**, starting from 2-phenylallyl 5-methoxy-1-oxo-2,3-dihydro-1*H*-indene-2-carboxylate (**1l**) (0.258 g, 0.800 mmol), 2-phenylallyl 2-cyano-5-methoxy-1-oxo-2,3-dihydro-1*H*-indene-2-carboxylate (**5h**) (0.139 g, 0.400 mmol, 50% yield) was obtained as a yellow oil.

R_F 0.5 (Pentane:Ethyl Acetate 4:1).

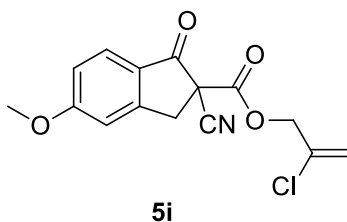
¹H NMR (400 MHz, Chloroform-*d*) δ 7.74 (d, J = 8.7 Hz, 1H, ArH), 7.39 – 7.29 (m, 5H, ArH), 6.98 (dd, J = 8.7, 2.2 Hz, 1H, ArH), 6.87 (d, J = 2.2 Hz, 1H, ArH), 5.55 (s, 1H, CCH₂), 5.43 (s, 1H, CCH₂), 5.18 – 5.05 (m, 2H, CH₂CPh), 3.92 (s, 3H, OMe), 3.66 (d, J = 17.3 Hz, 1H, CH₂), 3.50 (d, J = 16.8 Hz, 1H, CH₂).

¹³C NMR (101.00 MHz, Chloroform-*d*) δ 188.4, 167.2, 164.2, 154.8, 141.3, 137.7, 128.7, 128.4, 126.2, 125.2, 117.4, 116.2, 116.0, 109.6, 68.7, 56.2, 54.9, 37.5.

IR ν_{max} 2923 (w), 2853 (w), 2249 (w), 1749 (m), 1724 (s), 1599 (s), 1494 (w), 1265 (s), 1205 (m), 1092 (m), 908 (w).

HRMS (ESI) calcd for C₂₁H₁₇NNaO₄⁺ [M+Na]⁺ 370.1050; found 370.1047

2-Chloroallyl 2-cyano-5-methoxy-1-oxo-2,3-dihydro-1H-indene-2-carboxylate (**5i**)



Following general procedure **GP3**, starting from 2-chloroallyl 5-methoxy-1-oxo-2,3-dihydro-1H-indene-2-carboxylate (**1m**) (0.224 g, 0.798 mmol), 2-phenylallyl 2-cyano-5-methoxy-1-oxo-2,3-dihydro-1H-indene-2-carboxylate (**5i**) (0.095 g, 0.31 mmol, 39% yield) was obtained as a yellow oil.

R_F 0.27 (Pentane:Ethyl Acetate 4:1).

¹H NMR (400 MHz, Chloroform-*d*) 7.78 (d, J = 8.6 Hz, 1H, ArH), 7.01 (dd, J = 8.6, 2.3 Hz, 1H, ArH), 6.95 (m, 1H, ArH), 5.59 (s, 1H, CCH₂), 5.46 (s, 1H, CCH₂), 4.80 (q, J = 13.8 Hz, 2H, CH₂Cl), 3.94 (m, 4H, OMe + CH₂), 3.66 (d, J = 17.4 Hz, 1H, CH₂).

¹³C NMR (101.00 MHz, Chloroform-*d*) δ 187.9, 167.2, 163.7, 154.7, 133.8, 128.2, 124.8, 117.4, 115.7, 115.7, 109.6, 68.0, 56.1, 54.5, 37.4.

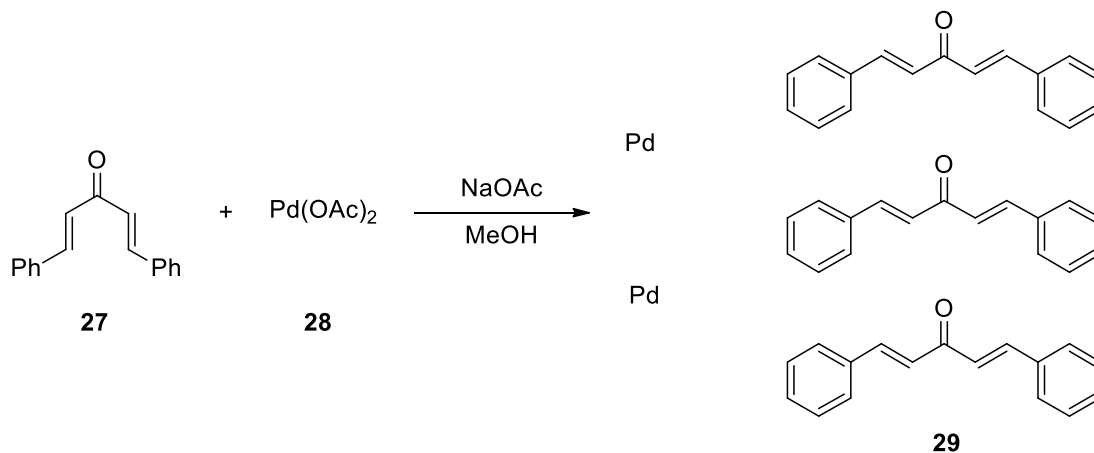
IR ν_{max} 2949 (w), 2845 (w), 2250 (w), 1756 (m), 1726 (s), 1604 (s), 1494 (w), 1449 (w), 1311 (m), 1269 (s), 1205 (m), 1093 (m).

HRMS (ESI) calcd for C₁₅H₁₃ClNO₄⁺ [M+H]⁺ 306.0528; found 306.0517.

5. Pd-Catalyzed decarboxylation of allyl β -keto esters.

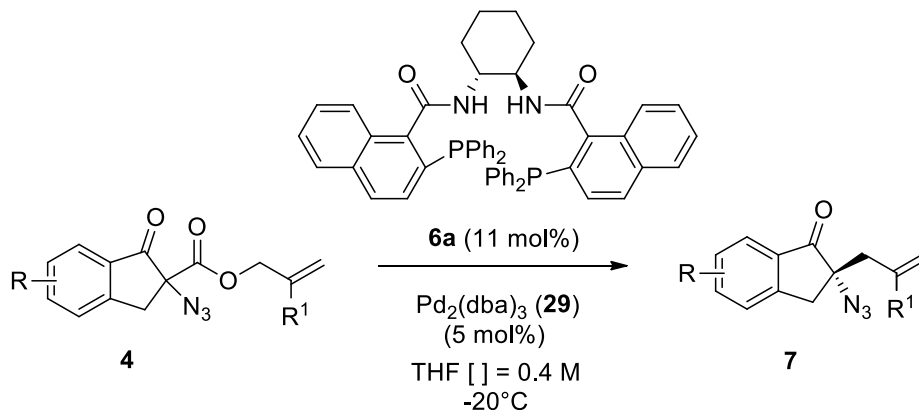
5.1 Synthesis of $\text{Pd}_2(\text{dba})_3$

$\text{Pd}_2(\text{dba})_3$ (**29**)



Following a reported procedure,¹⁹ palladium acetate (**28**) (0.20 g, 0.89 mmol) was placed into a 25 mL round-bottom flask with a magnetic stirrer. Sodium acetate (0.070 g, 0.89 mmol) was added followed by (1*E*,4*E*)-1,5-diphenylpenta-1,4-dien-3-one (**27**) (0.420 g, 1.78 mmol) and MeOH (10 mL). The reaction mixture was stirred at 40 °C for 3 h. After completion of the reaction a brown solid was formed. The solid was filtered off and washed with MeOH (2 x 3 mL) followed by water (3 x 3 mL). The residue was completely washed off the filter with CHCl_3 (25 mL), and the solution was evaporated on a rotary evaporator. The solid that formed was re-dissolved in a minimum amount of freshly distilled chloroform (ca. 5 mL), and 20 mL of acetone was added to the solution. The mixture that was obtained was left overnight in a refrigerator at -18 °C. The crystals of $\text{Pd}_2(\text{dba})_3 \cdot \text{CHCl}_3$ (**29**) (0.28 g, 0.31 mmol, 34% yield) were filtered off, washed with 2x5 mL of cold acetone (5 °C), and dried under vacuum at 40 °C.

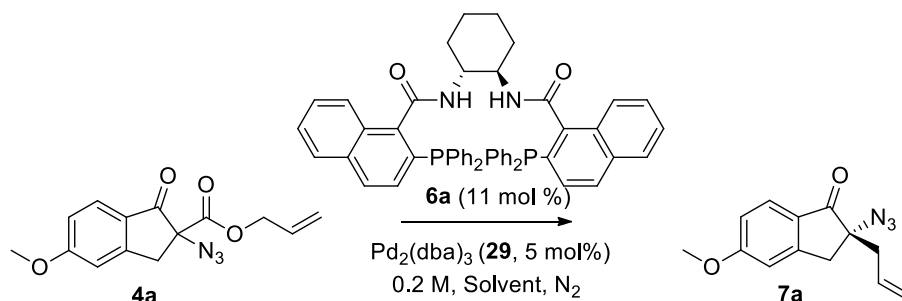
5.2 General procedure GP4 for the asymmetric decarboxylation of α -azido allyl β -keto esters catalyzed by Pd.



¹⁹ S.S. Zalesskiy, V.P. Ananikov, *Organometallics* **2012**, 31, 2302.

Substrate **4** (0.2 mmol), Pd₂(dba)₃ (**29**, 5 mol%) and ligand **6a** (11 mol%) were placed in a micro wave vial which was sealed. The solvent THF (0.5 mL) was added and the reaction was immediately degased three times. The mixture was placed in a refrigerator at -20 °C and monitored by TLC. Upon completeness (10-15 h) the reaction was filtered through a plug of silica and the solvent evaporated. Purification by column chromatography yielded the product that was analyzed by chiral HPLC. The procedure used for optimization and scope are the same.

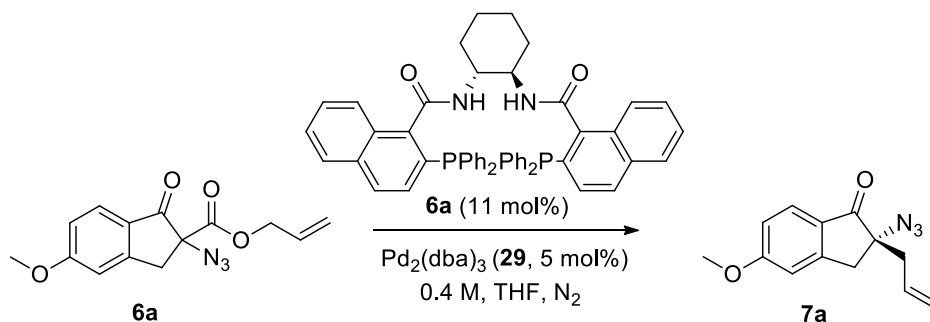
Supplementary Table S1 | Screening of the Solvent



| entry | solvent | NMR % Yield | e.e% ^a |
|-------|--------------------|-------------|-------------------|
| 1 | THF | 88 | 79% |
| 2 | DCM *(0 °C) | 60 | 63% |
| 3 | Toluene | 38 | 70% |
| 4 | CH ₃ CN | 50 | 68% |
| 5 | Et ₂ O | 27 | 71% |
| 6 | MTBE | 31 | 71% |
| 7 | Me-THF | 35 | 70% |
| 8 | THPyran | 35 | 70% |
| 9 | Dioxane | 38 | 42% |

a) Substrate **4a** (0.012 mmol), Pd₂(dba)₃ (**29** 5 mol%), **6a** (11 mol%) and solvent (0.2 M) at 25 °C. The ee are measured with chiral HPLC.

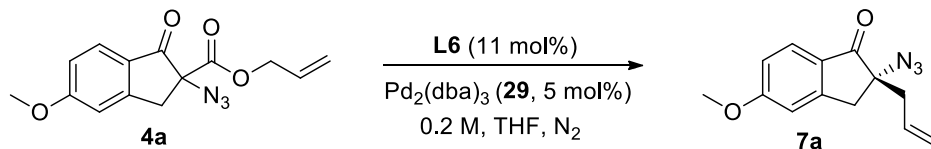
Supplementary Table S2 | Screening of the Temperature



| entry | temperature | NMR % Yield | e.e% ^a |
|-------|-------------|-------------|-------------------|
| 1 | -20°C | 88 | 86% |
| 2 | 0°C | 89 | 82% |
| 3 | 25°C | 80 | 82% |

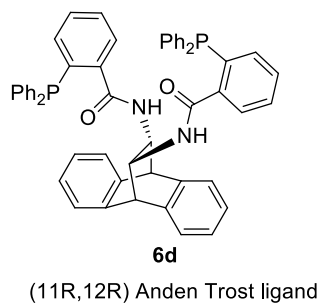
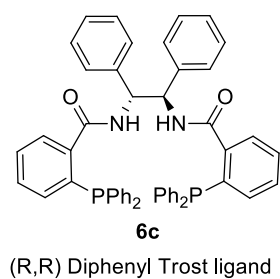
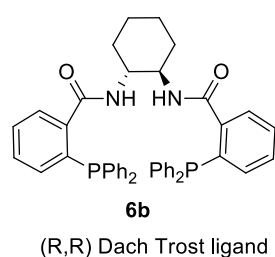
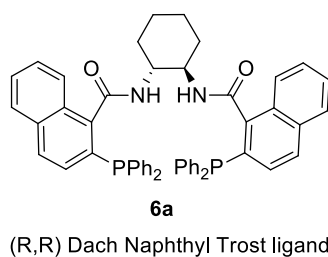
a) Substrate **4a** (0.012 mmol), Pd₂(dba)₃ (**29** 5 mol%), **6a** (11 mol%) and THF (0.4 M) at 25 °C. The *ee* are measured with chiral HPLC.

Supplementary Table S3 | Screening of Ligands

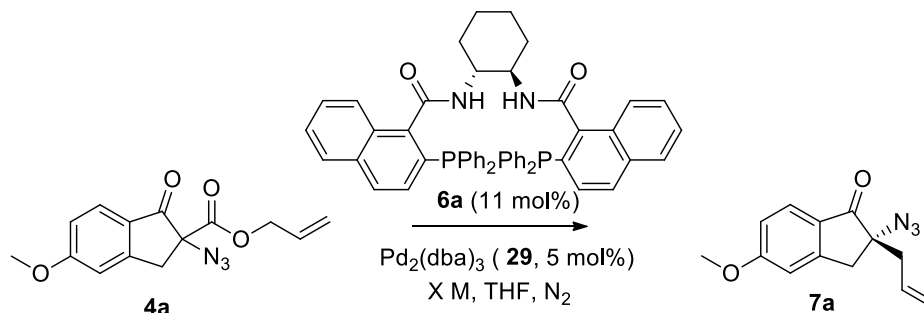


| entry | Ligand | NMR % Yield | e.e.% ^a |
|-------|-------------------------|-------------|--------------------|
| 1 | Dach 6b | 10 | 30% |
| 2 | Dach Naphthyl 6a | 88 | 79% |
| 3 | Anden 6d | 15 | 49% |
| 4 | DiPhenyl 6c | n.r. | - |
| 5 | Stoltz 6e | n.r | - |

a) Substrate **10a** (0.012 mmol), Pd₂(dba)₃ (**29** 5 mol%), L (11 mol%) and THF (0.4 M) at 25 °C. The *ee* are measured with chiral HPLC.



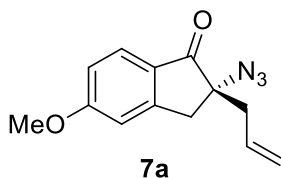
Supplementary Table S4 | Screening of Concentrations



| entry | Concentration | NMR % Yield | e.e. ⁰ % ^a |
|-------|---------------|-------------|----------------------------------|
| 1 | 0.1 M | 80 | 82% |
| 2 | 0.2 M | 88 | 79% |
| 3 | 0.4 M | 94 | 82% |

a) Substrate **4a** (0.012 mmol), Pd₂(dba)₃ (**29** 5 mol%), **6a** (11 mol%) and THF (X M) at 25 °C. The *ee* are measured with chiral HPLC.

(*R*)-2-Allyl-2-azido-5-methoxy-2,3-dihydro-1*H*-inden-1-one (**7a**)



Following general procedure **GP4**, starting from substrate **4a** (0.057 g, 0.20 mmol), (*R*)-2-allyl-2-azido-5-methoxy-2,3-dihydro-1*H*-inden-1-one (**7a**) (0.042 g, 0.17 mmol, 86% yield, 86% *ee*) was obtained as a yellow oil.

Chiral HPLC conditions: *ee*: 86%. Chiralcel IA 95:5 Hexane/*i*PrOH, 1 mL/min, 15 min *t*_{R1} = 8.9 min and *t*_{R2} = 10.5 min. λ = 280 cm⁻¹.

R_F 0.4 (Dichloromethane:Pentane 2:1).

¹H NMR (400 MHz, Chloroform-*d*) δ 7.73 (d, *J* = 8.6 Hz, 1H, Ar*H*), 6.94 (dd, *J* = 8.6, 2.2 Hz, 1H, Ar*H*), 6.83 (d, *J* = 2.2 Hz, 1H, Ar*H*), 5.73 (ddt, *J* = 17.2, 10.1, 7.2 Hz, 1H, CHCH₂), 5.29 – 5.08 (m, 2H, CHCH₂), 3.89 (s, 3H, OCH₃), 3.20 (d, *J* = 17.5 Hz, 1H, CH₂), 2.92 (d, *J* = 17.5 Hz, 1H, CH₂), 2.82 – 2.69 (m, 1H, CH₂CH), 2.61 – 2.47 (m, 1H, CH₂CH).

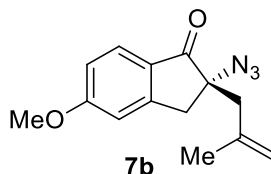
¹³C NMR (101 MHz, CDCl₃) δ 200.5, 166.4, 154.3, 131.3, 127.1, 126.8, 120.3, 116.2, 109.6, 67.8, 55.8, 39.0, 37.7.

IR ν_{max} 2939 (w), 2927 (w), 2844 (w), 2097 (s), 1708 (s), 1598 (s), 1265 (s), 1093 (m), 1024 (m), 927 (m).

HRMS (ESI) calcd for C₁₃H₁₃N₃NaO₂⁺ [M+Na]⁺ 266.0900; found 266.0898.

[α]_D^{25.0} +10.7 (*c* = 3.38, CHCl₃).

(R)-2-azido-5-methoxy-2-(2-methylallyl)-2,3-dihydro-1H-inden-1-one (7b)



Following general procedure **GP4**, starting from substrate **4b** (0.061 g, 0.20 mmol) (*R*)-5-methoxy-2-(2-methylallyl)-2-((triisopropylsilyl)ethynyl)-2,3-dihydro-1*H*-inden-1-one (**7b**) (0.066 mg, 0.26 mmol, 86% yield, 97% *ee*) was obtained as a yellow oil.

Chiral HPLC conditions. *ee*: 97%; Chiralcel IA 95:5 Hexane/*i*PrOH, 1 mL/min, 20 min. t_{R1} = 8.6 min and t_{R2} = 10.0 min. λ = 254 nm.

R_F 0.4 (Dichloromethane:Pentane 2:1).

¹H NMR (400 MHz, Chloroform-*d*) δ 7.72 (d, J = 8.6 Hz, 1H, Ar*H*), 6.93 (dd, J = 8.6, 2.2 Hz, 1H, Ar*H*), 6.82 (d, J = 2.2 Hz, 1H, Ar*H*), 4.92 (t, J = 1.7 Hz, 1H, CCH₂), 4.88 – 4.82 (m, 1H, CCH₂), 3.88 (s, 3H, OCH₃), 3.29 (d, J = 17.5 Hz, 1H, CH₂), 2.88 (d, J = 17.6 Hz, 1H, CH₂), 2.78 (d, J = 14.4 Hz, 1H, CH₂C), 2.49 (dd, J = 14.5, 1.0 Hz, 1H, CH₂C), 1.81 – 1.74 (m, 3H, CH₃).

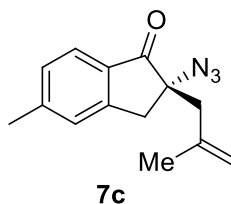
¹³C NMR (101 MHz, CDCl₃) δ 200.4, 166.4, 154.6, 140.3, 126.9, 126.7, 116.2, 116.0, 109.7, 67.6, 55.8, 41.5, 37.6, 23.4.

IR ν_{\max} 3076 (w), 3075 (w), 3016 (w), 3015 (w), 2970 (w), 2941 (w), 2940 (w), 2929 (w), 2928 (w), 2927 (w), 2845 (w), 2844 (w), 2101 (s), 1708 (s), 1600 (s), 1599 (s), 1445 (w), 1266 (s), 1093 (m), 1026 (w), 903 (m), 757 (s).

HRMS (ESI) calcd for C₁₄H₁₅N₃NaO₂⁺ [M+Na]⁺ 280.1056; found 280.1057.

[α]_D^{25.0} +15.3 (c = 3.86, CHCl₃).

(R)-2-Azido-5-methyl-2-(2-methylallyl)-2,3-dihydro-1H-inden-1-one (7c)



Following the general procedure **GP4**, starting from substrate **4c** (0.057 g, 0.20 mmol) (*R*)-2-azido-5-methyl-2-(2-methylallyl)-2,3-dihydro-1*H*-inden-1-one (**7c**) (0.039 g, 0.16 mmol, 81% yield, 96% *ee*) was obtained as a yellow oil.

Chiral HPLC conditions: *ee*: 96%; Chiralcel IA 95:5 Hexane/*i*PrOH, 1 mL/min, 10 min. t_{R1} = 5.7 min and t_{R2} = 6.6 min. λ = 280 nm.

R_F 0.85 (Pentane:Diethyl Ether 9:1).

¹H NMR (400 MHz, Chloroform-*d*) δ 7.70 (d, J = 7.8 Hz, 1H, Ar*H*), 7.25 – 7.19 (m, 2H, Ar*H*), 4.93 (t, J = 1.6 Hz, 1H, CMeCH₂), 4.85 (dd, J = 1.9, 1.0 Hz, 1H, CMeCH₂), 3.30 (d, J = 17.5 Hz, 1H, CH₂), 2.90 (d, J = 18.0 Hz, 1H, CH₂), 2.79 (dd, J = 14.4, 1.0 Hz, 1H, CH₂CMe), 2.50 (dd, J = 14.4, 1.1 Hz, 1H, CH₂CMe), 2.45 (s, 3H, ArCH₃), 1.77 (t, J = 1.1 Hz, 3H, CH₃).

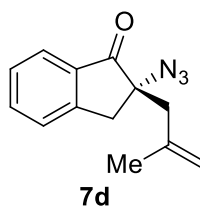
¹³C NMR (101 MHz, Chloroform-*d*) δ 201.9, 152.0, 147.6, 140.2, 131.4, 129.4, 126.9, 125.0, 116.1, 67.5, 41.5, 37.4, 23.5, 22.3.

IR ν_{max} 2943 (w), 2924 (w), 2852 (w), 2101 (s), 1715 (s), 1609 (s), 1255 (s), 1254 (s), 904 (m).

HRMS (ESI) calcd for C₁₄H₁₅N₃NaO⁺ [M+Na]⁺ 264.1107; found 264.1110.

[α]_D^{25.0} +10.4 (c = 2.78, CHCl₃).

(*R*)-2-Azido-2-(2-methylallyl)-2,3-dihydro-1*H*-inden-1-one (7d)



Following the general procedure **GP4**, starting from substrate **4d** (0.054 g, 0.20 mmol) (*R*)-2-Azido-2-(2-methylallyl)-2,3-dihydro-1*H*-inden-1-one (**7d**) (0.035 g, 0.15 mmol, 77% yield, 95% *ee*) was obtained as a yellow oil.

Chiral HPLC conditions: *ee*: 95%; Chiralcel IA 99:1 Hexane/*i*PrOH, 1 mL/min, 15 min t_{R1} = 7.0 min and t_{R2} = 8.4 min. λ = 254 nm.

R_F 0.33 (Pentane:Ethyl Acetate 95:5).

¹H NMR (400 MHz, Chloroform-*d*) δ 7.81 (dd, J = 7.9, 1.1 Hz, 1H, Ar*H*), 7.64 (td, J = 7.5, 1.3 Hz, 1H, Ar*H*), 7.48 – 7.37 (m, 2H, Ar*H*), 4.94 (m, 1H, CCH₂), 4.86 (m, 1H, CCH₂), 3.35 (d, J = 17.5 Hz, 1H, CH₂), 2.95 (d, J = 17.5 Hz, 1H, CH₂), 2.81 (dd, J = 14.5, 1.0 Hz, 1H, CH₂C), 2.51 (dd, J = 14.6, 1.0 Hz, 1H, CH₂C), 1.77 (t, J = 1.1 Hz, 3H, CH₃).

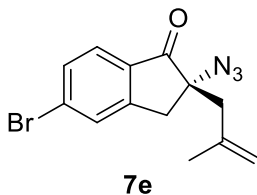
¹³C NMR (101 MHz, Chloroform-*d*) δ 202.4, 151.5, 140.1, 136.1, 133.7, 128.2, 126.6, 125.2, 116.2, 67.3, 41.4, 37.6, 23.5.

IR ν_{max} 3076 (w), 2928 (w), 2856 (w), 2101 (s), 1718 (s), 1606 (m), 1301 (w), 1255 (m), 1222 (w), 908 (s), 734 (s).

HRMS (ESI) calcd for C₁₃H₁₃N₃NaO⁺ [M+Na]⁺ 250.0951; found 250.0949.

[α]_D^{25.0} +10.5 (c = 2.83, CHCl₃).

(R)-2-Azido-5-bromo-2-(2-methylallyl)-2,3-dihydro-1H-inden-1-one (7e)



Following general procedure **GP4**, starting from substrate **4e** (0.070 g, 0.20 mmol) (*R*)-2-azido-5-bromo-2-(2-methylallyl)-2,3-dihydro-1*H*-inden-1-one (**7e**) (0.052 g, 0.17 mmol, 85% yield, 90% *ee*) was obtained as a yellow oil.

Chiral HPLC conditions: *ee*: 90%; Chiralcel IA 99:1 Hexane/*i*PrOH, 1 mL/min, 15 min t_{R1} = 8.9 min and t_{R2} = 10.6 min. λ = 254 nm.

R_F 0.7 (Pentane:Ethyl Acetate 95:5).

¹H NMR (400 MHz, Chloroform-*d*) δ 7.67 (dd, J = 8.2, 0.6 Hz, 1H, Ar*H*), 7.62 – 7.52 (m, 2H, Ar*H*), 4.94 (t, J = 1.6 Hz, 1H, CMeCH₂), 4.87 – 4.80 (m, 1H, CMeCH₂), 3.33 (dd, J = 17.6, 0.7 Hz, 1H, CH₂), 2.92 (d, J = 17.7 Hz, 1H, CH₂), 2.79 (dd, J = 14.5, 1.1 Hz, 1H, CH₂CMe), 2.52 (dd, J = 14.4, 1.0 Hz, 1H, CH₂CMe), 1.76 (dd, J = 1.5, 0.8 Hz, 3H, CH₃).

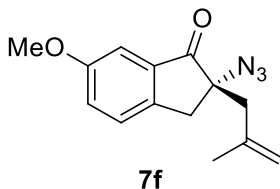
¹³C NMR (101 MHz, Chloroform-*d*) δ . 201.3, 153.0, 139.8, 132.5, 131.9, 131.6, 129.9, 126.3, 116.4, 67.3, 41.3, 37.2, 23.5.

IR ν_{\max} 3079 (w), 2927 (w), 2857 (w), 2105 (s), 1724 (s), 1596 (s), 1251 (m), 1215 (m), 907 (m).

HRMS (ESI) calcd for C₁₃H₁₃⁷⁹BrNO⁺ [M-N₂+H]⁺ 278.0175; found 278.0180.

[α]_D^{25.0} +12.4 (c = 4.26, CHCl₃).

(R)-2-Azido-6-methoxy-2-(2-methylallyl)-2,3-dihydro-1H-inden-1-one (7f)



Following general procedure **GP4**, starting from substrate **4f** (0.060 g, 0.20 mmol), (*R*)-2-azido-6-methoxy-2-(2-methylallyl)-2,3-dihydro-1*H*-inden-1-one (**7f**) (0.029 g, 0.11 mmol, 56% yield, 89% *ee*) was obtained as a yellow oil.

Chiral HPLC conditions: *ee*: 89%; Chiralcel IC 99.9:0.1 Hexane/*i*PrOH, 1 mL/min, 20 min t_{R1} = 5.4 min and t_{R2} = 5.9 min, λ = 280 nm.

R_F 0.65 (Pentane:Ethyl Acetate 9:1).

¹H NMR (400 MHz, Chloroform-*d*) δ 7.30 (ddd, J = 8.0, 1.7, 0.9 Hz, 1H, Ar*H*), 7.25 – 7.21 (m, 2H, Ar*H*), 4.93 (t, J = 1.6 Hz, 1H, CMeCH₂), 4.85 (d, J = 1.0 Hz, 1H, CMeCH₂), 3.84 (s, 3H, OMe), 3.27 (dd, J = 17.2, 0.8 Hz, 1H, CH₂), 2.88 (d, J = 16.9 Hz, 1H, CH₂), 2.79 (dd, J = 14.5, 1.1 Hz, 1H, CH₂CMe), 2.51 (dd, J = 14.5, 1.1 Hz, 1H, CH₂CMe), 1.76 (t, J = 1.1 Hz, 3H, CH₃).

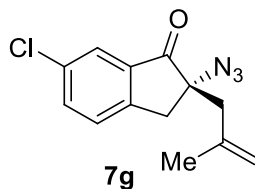
¹³C NMR (101 MHz, Chloroform-*d*) δ 202.4, 159.9, 144.4, 140.1, 134.8, 127.3, 125.6, 116.1, 106.0, 68.1, 55.7, 41.5, 37.0, 23.5.

IR ν_{max} 3075 (w), 2933 (w), 2841 (w), 2103 (s), 1717 (s), 1491 (s), 1437 (m), 1276 (s), 1242 (s), 902 (m), 771 (m).

HRMS (ESI) calcd for C₁₄H₁₅N₃NaO₂⁺ [M+Na]⁺ 280.1056; found 280.1060.

[α]_D^{25.0} +3.1 (c = 1.03, CHCl₃).

(*R*)-2-Azido-6-chloro-2-(2-methylallyl)-2,3-dihydro-1*H*-inden-1-one (7g)



Following general procedure **GP4**, starting from substrate **4g** (0.061 mg, 0.20 mmol) (*R*)-2-azido-6-chloro-2-(2-methylallyl)-2,3-dihydro-1*H*-inden-1-one (**7g**) (0.046 g, 0.18 mmol, 88% yield, 87% *ee*) was obtained as a yellow oil.

Chiral HPLC conditions: *ee*: 87%; Chiralcel IA 99:1 Hexane/*i*PrOH, 1 mL/min, 20 min t_{R1} = 6.4 min and t_{R2} = 7.9 min. λ = 254 nm.

R_F 0.6 (Pentane:Dichloromethane 1:1).

¹H NMR (400 MHz, Chloroform-*d*) δ 7.76 (d, J = 2.0 Hz, 1H, Ar*H*), 7.59 (dd, J = 8.2, 2.1 Hz, 1H, Ar*H*), 7.36 (d, J = 8.2 Hz, 1H, Ar*H*), 4.94 (t, J = 1.6 Hz, 1H, CMeCH₂), 4.85 (dd, J = 1.9, 1.0 Hz, 1H, CMeCH₂), 3.30 (d, J = 17.6 Hz, 1H, CH₂), 2.90 (d, J = 17.6 Hz, 1H, CH₂), 2.79 (dd, J = 14.5, 1.0 Hz, 1H, CH₂CMe), 2.51 (dd, J = 14.5, 1.1 Hz, 1H, CH₂CMe), 1.76 (t, J = 1.1 Hz, 3H, CH₃).

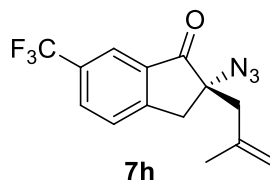
¹³C NMR (101 MHz, Chloroform-*d*) δ 201.2, 149.6, 139.8, 136.1, 135.2, 134.5, 127.8, 124.8, 116.4, 67.8, 41.3, 37.2, 23.5.

IR ν_{max} 3080 (w), 2925 (w), 2102 (s), 1723 (s), 1469 (w), 1430 (m), 1429 (m), 1285 (w), 1250 (m), 1208 (m), 1186 (m), 903 (m), 822 (w), 821 (w), 737 (w).

HRMS (ESI) calcd for C₁₃H₁₃ClNO [M-N₂+H]⁺ 234.0686; found 234.0688.

[α]_D^{25.0} +11.7 (c = 3.52, CHCl₃).

(R)-2-Azido-2-(2-methylallyl)-6-(trifluoromethyl)-2,3-dihydro-1H-inden-1-one (7h)



Following general procedure **GP4**, starting from substrate **4h** (0.076 g, 0.22 mmol), (*R*)-2-azido-2-(2-methylallyl)-6-(trifluoromethyl)-2,3-dihydro-1*H*-inden-1-one (**7h**) (0.033 g, 0.11 mmol, 50% yield, 77% *ee*) was obtained as a brown oil.

Chiral HPLC conditions: *ee*: 77%; Chiralcel IA 99:1 Hexane/*i*PrOH, 1 mL/min, 10 min. t_{R1} = 5.3 min and t_{R2} = 6.2 min, λ = 254 nm.

R_F 0.35 (Pentane:Dichloromethane 2:1).

¹H NMR (400 MHz, Chloroform-*d*) δ 8.07 (d, J = 1.7 Hz, 1H, Ar*H*), 7.88 (dd, J = 8.1, 1.7 Hz, 1H, Ar*H*), 7.57 (d, J = 8.0 Hz, 1H, Ar*H*), 4.99 – 4.91 (m, 1H, CMeCH₂), 4.92 – 4.82 (m, 1H, CMeCH₂), 3.40 (d, J = 17.9 Hz, 1H, CH₂), 3.00 (d, J = 17.9 Hz, 1H, CH₂), 2.82 (dd, J = 14.6, 1.0 Hz, 1H, CH₂CMe), 2.54 (dd, J = 14.5, 1.1 Hz, 1H, CH₂CMe), 1.77 (t, J = 1.1 Hz, 3H, CH₃).

¹³C NMR (101 MHz, Chloroform-*d*) δ 201.3, 154.7, 139.7, 134.2, 132.4, 131.0 (q, J = 33.2 Hz), 127.4, 123.5 (q, J = 272.9 Hz), 122.4, 116.5, 67.5, 41.1, 37.7, 23.5.

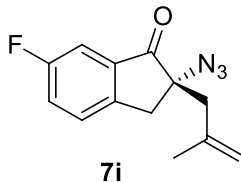
¹⁹F NMR (376 MHz, Chloroform-*d*) δ -62.2.

IR ν_{\max} 3019 (w), 2970 (w), 2939 (w), 2930 (w), 2103 (m), 1708 (m), 1600 (m), 1266 (s), 1221 (m), 756 (s).

HRMS (ESI) calcd for C₁₃H₁₁F₃N₃O⁺ [M+H]⁺ 282.0849; found 282.0844.

[α]_D^{25.0} +6.5 (c = 2.8, CHCl₃).

(R)-2-azido-6-fluoro-2-(2-methylallyl)-2,3-dihydro-1H-inden-1-one (7i)



Following general procedure **GP4**, starting from substrate **4i** (0.058 g, 0.20 mmol), (*R*)-2-azido-6-fluoro-2-(2-methylallyl)-2,3-dihydro-1*H*-inden-1-one (**7i**) (0.036 g, 0.15 mmol, 73% yield, 92% *ee*) was obtained as a yellow oil.

Chiral HPLC conditions: *ee*: 92%; Chiralcel IA 99:1 Hexane/*i*PrOH, 1 mL/min, 30 min. t_{R1} = 6.3 min and t_{R2} = 6.9 min. λ = 230 nm

R_F 0.3 (Pentane: Dichloromethane 2:1).

¹H NMR (400 MHz, Chloroform-*d*) δ 7.44 (dd, $J = 7.2, 2.4$ Hz, 1H, Ar*H*, Ar*H*), 7.42 – 7.32 (m, 2H, Ar*H*), 4.94 (t, $J = 1.6$ Hz, 1H, CMeCH₂), 4.85 (dt, $J = 2.0, 1.0$ Hz, 1H, CMeCH₂), 3.31 (d, $J = 17.3$ Hz, 1H, CH₂), 2.91 (d, $J = 17.4$ Hz, 1H, CH₂), 2.79 (dd, $J = 14.4, 1.0$ Hz, 1H, CH₂CMe), 2.52 (dd, $J = 14.6, 1.0$ Hz, 1H, CH₂CMe), 1.76 (s, 3H, CH₃).

¹³C NMR (101 MHz, Chloroform-*d*) δ 201.7, 162.6 (d, $J = 249.4$ Hz), 147.0, 139.8, 135.4, 128.1, 123.9 (d, $J = 23.8$ Hz), 116.4, 110.9 (d, $J = 22.0$ Hz), 68.1, 41.3, 37.1, 23.5.

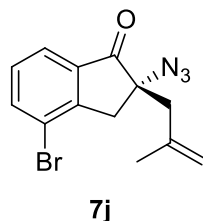
¹⁹F NMR (376 MHz, Chloroform-*d*) δ -113.0.

IR ν_{max} 3076 (w), 2929 (w), 2858 (w), 2104 (m), 1723 (m), 1488 (m), 1441 (w), 1265 (m), 1227 (m), 1226 (m), 758 (s).

HRMS (ESI) calcd for C₁₃H₁₃FNO⁺ [M-N₂+H]⁺ 218.0976; found 218.0980.

$[\alpha]_{\text{D}}^{25.0}$ +10.5 ($c = 3.11$, CHCl₃).

(*R*)-2-Azido-4-bromo-2-(2-methylallyl)-2,3-dihydro-1*H*-inden-1-one (7j)



Following general procedure **GP4**, starting from substrate **4j** (0.070 g, 0.20 mmol), (*R*)-2-azido-4-bromo-2-(2-methylallyl)-2,3-dihydro-1*H*-inden-1-one (**7j**) (0.052 g, 0.12 mmol, 85% yield, 87% *ee*) was obtained as a yellow oil.

Chiral HPLC conditions: *ee*: 87%; Chiralcel IA 99:1 Hexane/*i*PrOH, 1 mL/min, 10 min $t_{\text{R}1} = 5.5$ min and $t_{\text{R}2} = 6.2$ min, $\lambda = 254$ nm.

R_F 0.75 (Pentane:Ethyl Acetate 95:5).

¹H NMR (400 MHz, Chloroform-*d*) δ 7.81 (dd, $J = 7.8, 1.0$ Hz, 1H, Ar*H*), 7.77 (dd, $J = 7.6, 0.9$ Hz, 1H, Ar*H*), 7.38 – 7.29 (m, 1H, Ar*H*), 5.00 – 4.94 (m, 1H, CMeCH₂), 4.89 (dd, $J = 1.8, 0.9$ Hz, 1H, CMeCH₂), 3.27 (d, $J = 18.0$ Hz, 1H, CH₂), 2.89 (d, $J = 18.0$ Hz, 1H, CH₂), 2.83 (dd, $J = 14.5, 1.1$ Hz, 1H, CH₂CMe), 2.53 (dd, $J = 14.6, 1.1$ Hz, 1H, CH₂CMe), 1.78 (s, 2H, CH₃).

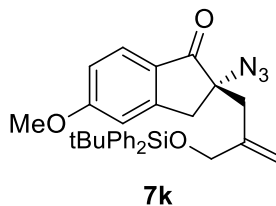
¹³C NMR (101 MHz, Chloroform-*d*) δ 201.8, 151.3, 139.6, 138.8, 135.7, 129.9, 123.9, 122.0, 116.5, 67.2, 41.2, 38.8, 23.5.

IR ν_{max} 3076 (w), 3020 (w), 2941 (w), 2846 (w), 2103 (m), 1709 (w), 1602 (m), 1333 (w), 1267 (m), 1219 (m), 1135 (w), 1109 (w), 1095 (w), 905 (w), 756 (s).

HRMS (ESI) calcd for C₁₃H₁₂NO⁷⁹Br⁺ [M-N₂]⁺ 280.0161; found 280.0165.

$[\alpha]_{\text{D}}^{25.0}$ +4.0 ($c = 1.58$, CHCl₃).

(S)-2-Azido-2-(2-(((tert-butyldiphenylsilyl)oxy)methyl)allyl)-5-methoxy-2,3-dihydro-1H-inden-1-one (7k)



Following general procedure **GP4**, starting from substrate **4k** (0.11 g, 0.20 mmol), (S)-2-azido-2-(2-(((tert-butyldiphenylsilyl)oxy)methyl)allyl)-5-methoxy-2,3-dihydro-1H-inden-1-one (**7k**) (0.052 g, 0.10 mmol, 51 % yield, 97% *ee*) was obtained as a yellow oil.

Chiral HPLC conditions: *ee*: 97%; Chiralcel IA 95:5 Hexane/*i*PrOH, 1 mL/min, 15 min t_{R1} = 7.0 min and t_{R2} = 8.4 min. λ = 254 nm⁻¹.

R_F 0.37 (Dichloromethane:Pentane 5:1).

¹H NMR (400 MHz, Chloroform-*d*) δ 7.70 (d, J = 8.6 Hz, 1H, ArH), 7.65 (m, 4H, *Ph*), 7.47 – 7.34 (m, 6H, *Ph*), 6.92 (dd, J = 8.6, 2.3 Hz, 1H, ArH), 6.77 (d, J = 2.2 Hz, 1H, ArH), 5.36 (d, J = 1.7 Hz, 1H, CCH₂), 5.08 (d, J = 1.3 Hz, 1H, CCH₂), 4.20 (d, J = 14.2 Hz, 1H, CH₂OTBDPS), 4.10 (d, J = 14.3 Hz, 1H, CH₂OTBDPS), 3.88 (s, 3H, OMe), 3.26 (d, J = 17.5 Hz, 1H, CH₂), 2.81 (d, J = 17.7 Hz, 1H, CH₂), 2.80 (d, J = 14.9 Hz, 1H, CH₂CCH₂), 2.51 (dd, J = 14.9, 1.0 Hz, 1H, CH₂CCH₂), 1.06 (s, 9H, *t*Bu).

¹³C NMR (101 MHz, Chloroform-*d*) δ 200.2, 166.4, 154.6, 142.6, 135.5, 135.5, 133.4, 133.4, 129.7, 127.7, 126.9, 126.7, 116.2, 114.4, 109.7, 67.7, 66.7, 55.8, 37.8, 36.7, 26.9, 19.3.²⁰

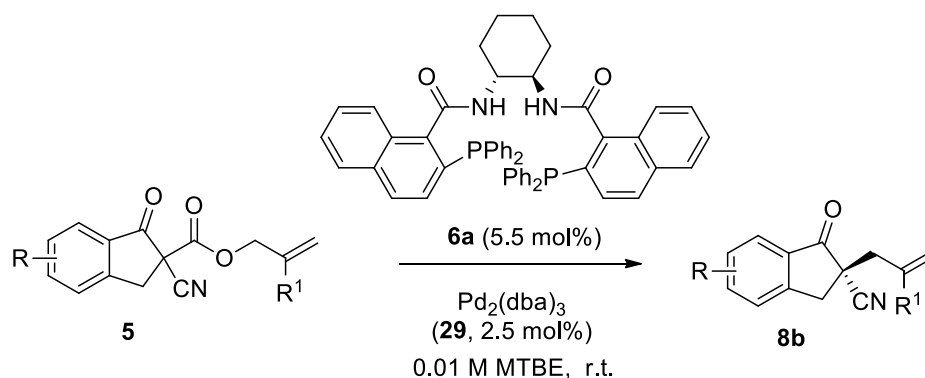
IR ν_{max} 2950 (w), 2102 (m), 1709 (m), 1600 (s), 1266 (s), 1109 (s), 912 (m), 824 (s).

HRMS (ESI) calcd for C₃₀H₃₃N₃NaO₃Si⁺ [M+Na]⁺ 534.2183; found 534.2177.

[α]_D^{25.0} +8.10 (*c* = 4.40, CHCl₃).

5.3 General procedure GP5 for the asymmetric decarboxylation of α -cyano allyl β -keto esters catalyzed by Pd.

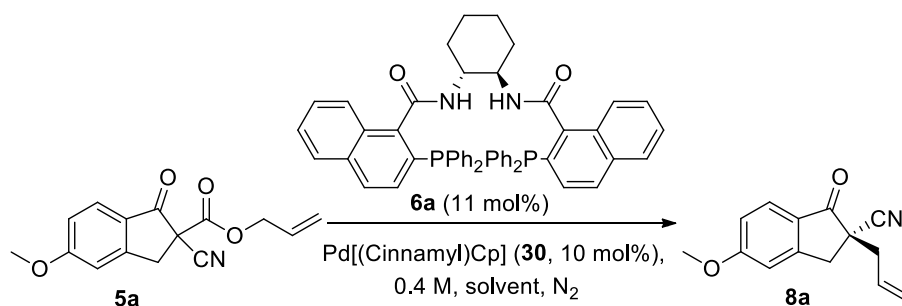
²⁰ Two C in the aromatic region are not resolved.



Substrate **5** (0.2 mmol), $\text{Pd}_2(\text{dba})_3$ (**29**, 2.5 mol%) and ligand **6a** (5.5 mol%) were placed in a micro wave vial which was sealed. The solvent MTBE (20 mL, 0.01M) was added and the reaction was immediately degassed three times. The reaction was then monitored by TLC. After 12 hours the starting material was consumed and the solvent evaporated. Purification by column chromatography using the solvent mixture indicated for the R_F of each compound yielded the product that was analyzed by chiral HPLC. The procedure used for optimization and scope is the same.

Reaction Optimization for Allyl substrate

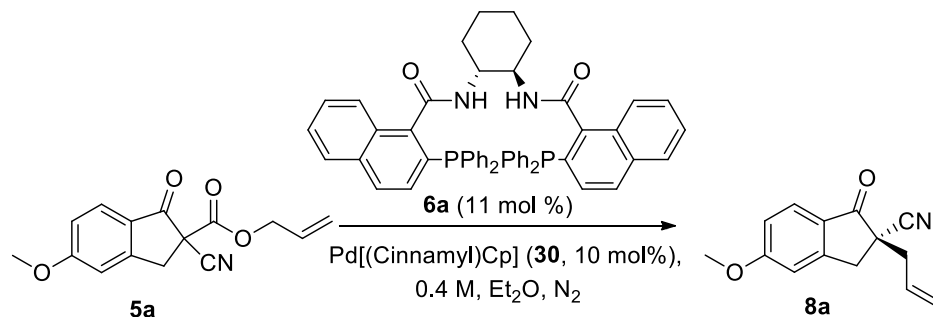
Supplementary Table S5 | Screening of the Solvent



| Entry | Solvent | Yield% ^a | ee% ^a |
|----------|---|---------------------|--------------------------|
| 1 | THF | 99 | 68 |
| 2 | DCM | 95 | 50 |
| 3 | Toluene | n.r. | - |
| 4 | CH_3CN | 82 | 45 |
| 5 | Et_2O | 98 | 61-78^b |
| 6 | MTBE | 93 | 70 |
| 7 | $i\text{Pr}_2\text{O}$ | 99 | 71 |
| 8 | $n\text{Bu}_2\text{O}$ | >99 | 67 |
| 9 | Ph_2O | 94 | 49 |
| 10 | dioxane | 94 | 39 |

a) Substrate **5a** (0.037 mmol), $\text{Pd}[(\text{Cinnamyl})\text{Cp}]$ (**30**, 10 mol%), **6a** (11 mol%) and solvent (0.4 M) at 25 °C. Isolated yield after flash chromatography is given, the ee are measured with chiral HPLC. b) Not reproducible.

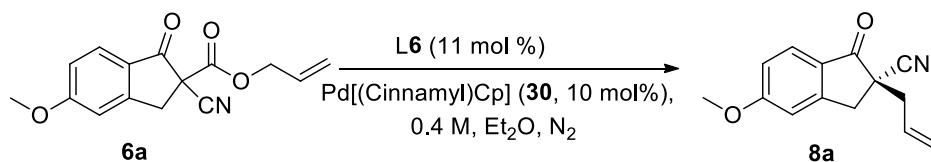
Supplementary Table S6 | Screening of the Temperature



| Entry | Temperature | Yield% | <i>ee</i> % ^a |
|-------|-------------|--------|--------------------------|
| 1 | -20°C | 97 | 57 |
| 2 | 0°C | 98 | 59 |
| 3 | r.t | 98 | 78 |
| 4 | 40°C | >99 | 57 |

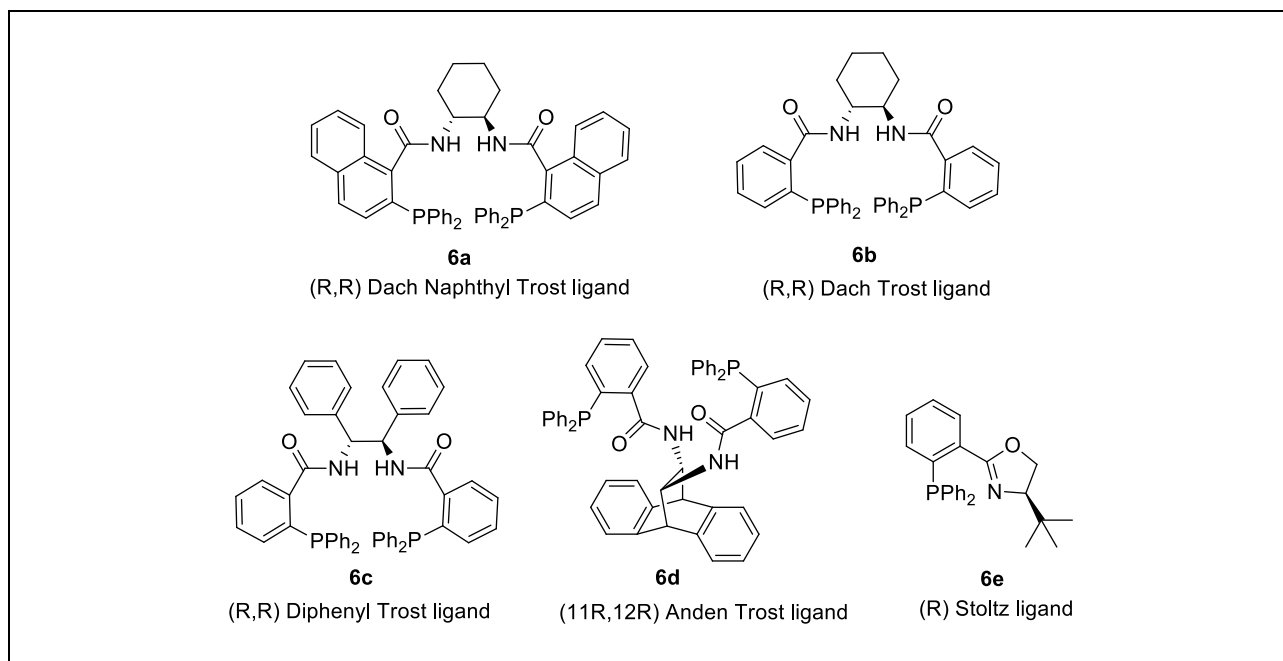
a) Substrate **5a** (0.037 mmol), Pd[(Cinnamyl)Cp] (**30**, 10 mol%), **6a** (11 mol%) and Et₂O (0.4 M). Isolated yield after flash chromatography is given, the *ee* are measured with chiral HPLC.

Supplementary Table S7 | Screening of Ligands

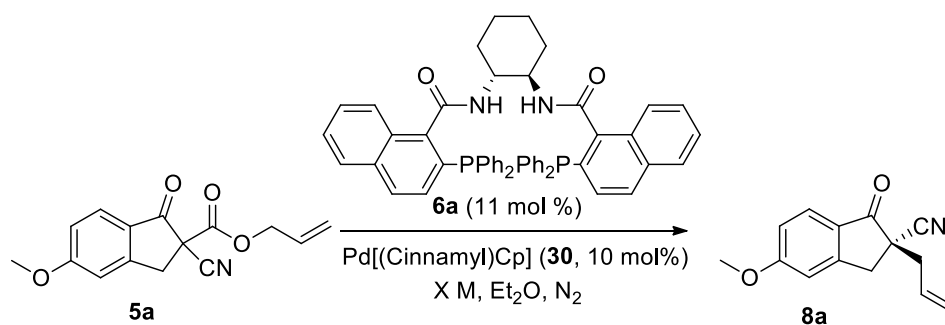


| Entry | Ligand | Yield% | <i>ee</i> % ^a |
|-------|------------------------|--------|--------------------------|
| 1 | Stoltz 6e | 94 | 0 |
| 2 | Dach 6b | 92 | 23 |
| 3 | Dach Naphtyl 6a | 98 | 78 |
| 4 | Anden 6d | 94 | 31 |
| 5 | DiPhenyl 6c | >99 | 47 |

a) Substrate **11a** (0.037 mmol), Pd[(Cinnamyl)Cp] (**34**, 10 mol%), L (11 mol%) and Et₂O (0.4 M) at 25 °C. Isolated yield after flash chromatography is given, the *ee* are measured with chiral HPLC.



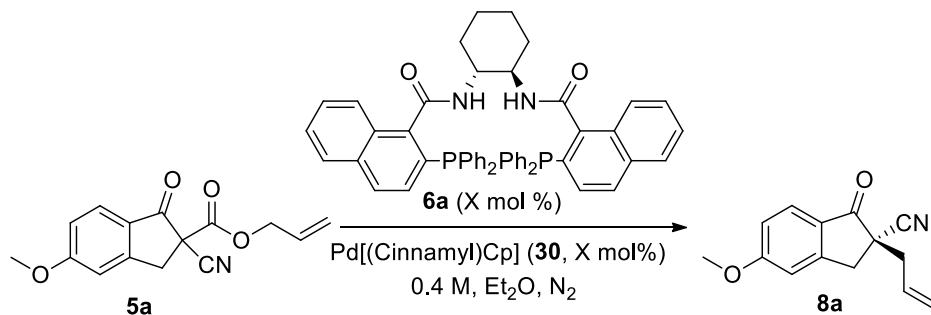
Supplementary Table S8 | Screening of Concentrations



| Entry | Concentration | Yield% | ee % ^a |
|----------|---------------|-----------|-------------------|
| 1 | 0.04 M | 98 | 59 |
| 2 | 0.1 M | 98 | 61 |
| 3 | 0.3 M | 93 | 55 |
| 4 | 0.4 M | 98 | 78 |
| 5 | 0.5 M | 91 | 41 |
| 6 | 1 M | 91 | 49 |

a) Substrate **5a** (0.037 mmol), Pd[(Cinnamyl)Cp] (**30**, 10 mol%), **6a** (11 mol%) and Et₂O (X M) at 25 °C. Isolated yield after flash chromatography is given, the ee are measured with chiral HPLC.

Supplementary Table S9 | Pd:Ligand loading and ratio

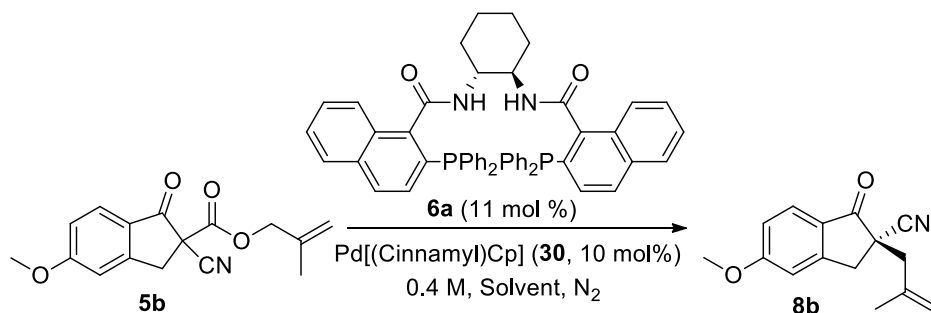


| Entry | Pd:Ligand | Yield% | <i>ee</i> % ^a |
|----------|---------------|-------------------|--------------------------|
| 1 | 2.5/2.75% | n.r. ^b | - |
| 2 | 5/5.5% | 92 | 47 |
| 3 | 5/10% | 97 | 43 |
| 4 | 5/20% | 93 | 49 |
| 5 | 10/11% | 98 | 78 |

a) Substrate **5a** (0.037 mmol), $\text{Pd}[(\text{Cinnamyl})\text{Cp}]$ (**30**, X mol%), **6a** (X mol%) and Et_2O (0.4 M) at 25 °C. Isolated yield after flash chromatography is given, the *ee* are measured with chiral HPLC. b) No complete conversion after 48 hours.

Reaction Optimization for Methylallyl Substrate

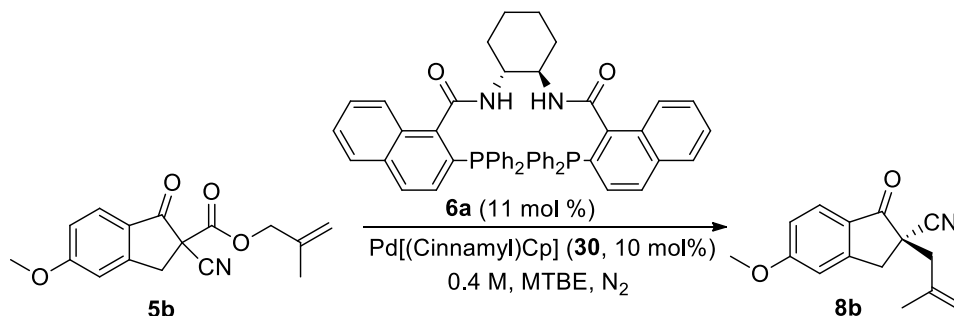
Supplementary Table S10 | Screening of the Solvent



| Entry | Solvent | Yield% | <i>ee</i> % ^a |
|----------|--------------------------|-----------|--------------------------|
| 1 | THF | 84 | 60 |
| 2 | DCM | 77 | 70 |
| 3 | Toluene | 86 | 68 |
| 4 | CH_3CN | 82 | 61 |
| 5 | Et_2O | 71 | 79 |
| 6 | MTBE | 89 | 78 |
| 7 | Methyl-Cyclopentyl ether | 94 | 53 |
| 8 | DMF | 80 | 42 |
| 9 | DMSO | 78 | 29 |

a) Substrate **5b** (0.035 mmol), Pd[(Cinnamyl)Cp] (**30**, 10 mol%), **6a** (11 mol%) and solvent (0.4 M) at 25 °C. Isolated yield after flash chromatography is given, the *ee* are measured with chiral HPLC.

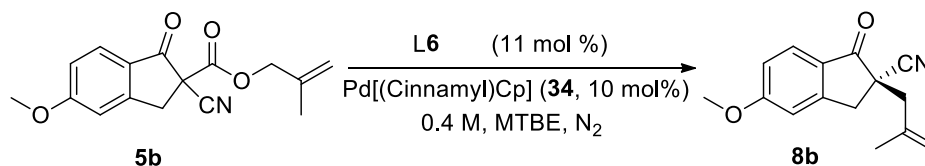
Supplementary Table S11 | Screening of the Temperature



| Entry | Temperature | Yield% | <i>ee</i> % ^a |
|-------|-------------|-----------|--------------------------|
| 1 | -10°C | 84 | 72% |
| 2 | 0°C | 83 | 59% |
| 3 | r.t. | 89 | 78% |
| 4 | 40°C | 82 | 74% |

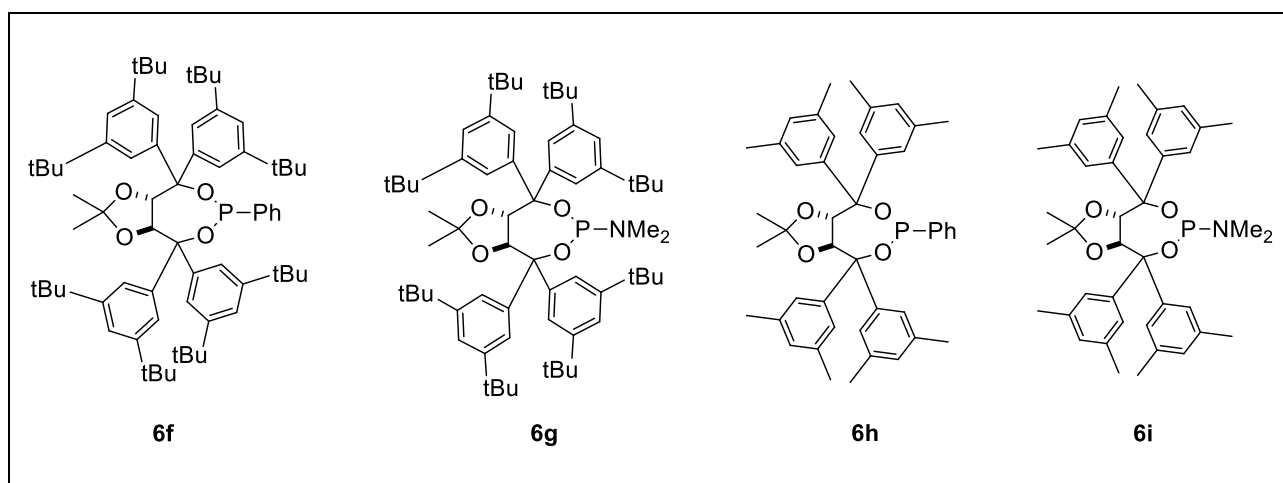
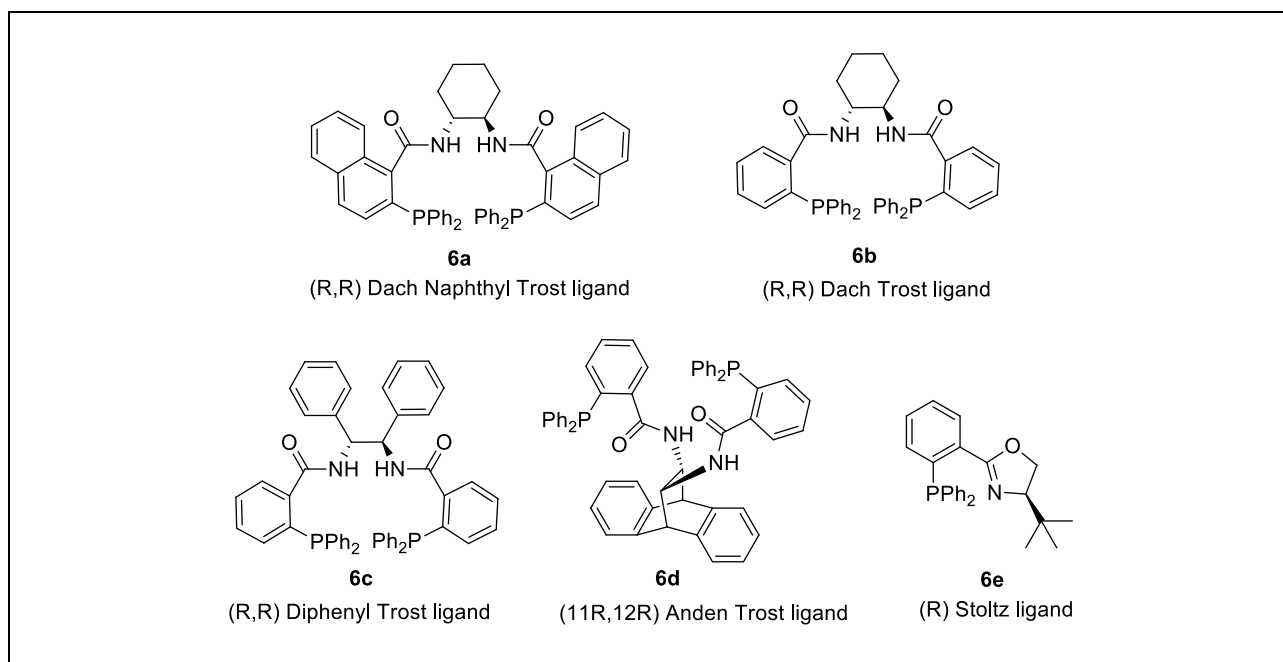
a) Substrate **5b** (0.035 mmol), Pd[(Cinnamyl)Cp] (**30**, 10 mol%), **6a** (11 mol%) and MTBE (0.4 M). Isolated yield after flash chromatography is given, the *ee* are measured with chiral HPLC.

Supplementary Table S12 | Screening of Ligands

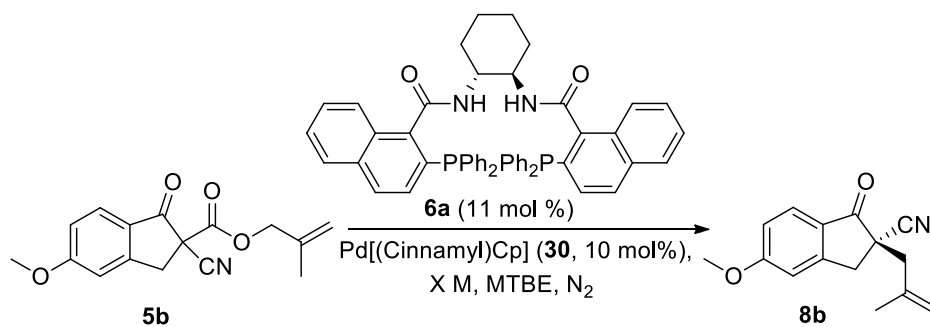


| Entry | Ligand | Yield% | <i>ee</i> % ^a |
|-------|------------------------|-------------------|--------------------------|
| 1 | Stoltz 6e | 86 | 1.4% |
| 2 | Dach 6b | 83 | 48% |
| 3 | Dach Naphtyl 6a | 89 | 78% |
| 4 | Anden 6c | 84 | 40% |
| 5 | DiPhenyl 6d | 82 | 41% |
| 6 | 6f | 95 | 1.6% |
| 7 | 6g | n.r. ^b | - |
| 8 | 6h | 90 | 38% |
| 9 | 6i | 85 | 25% |

a) Substrate **5b** (0.035 mmol), Pd[(Cinnamyl)Cp] (**30**, 10 mol%), L (11 mol%) and MTBE (0.4 M) at 25 °C. Isolated yield after flash chromatography is given, the *ee* are measured with chiral HPLC. b) No complete conversion after 48 hours.



Supplementary Table S13 | Screening of Concentrations

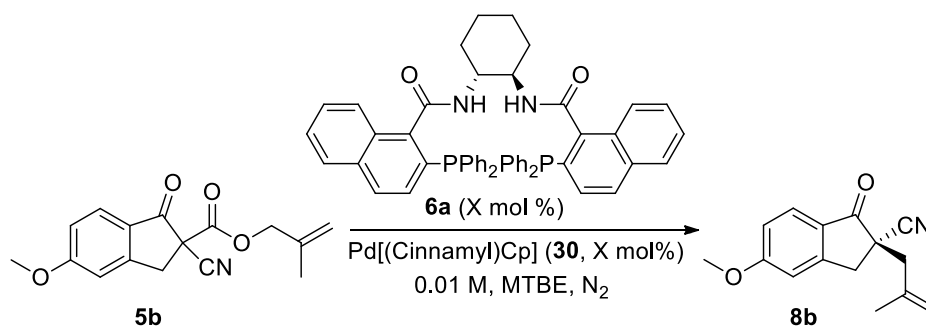


| Entry | Concentration | Yield% | ee % ^a |
|-------|---------------|--------|-------------------|
|-------|---------------|--------|-------------------|

| | | | |
|----------|---------------|-----------|------------|
| 1 | 0.001 M | 92 | 60% |
| 2 | 0.005 M | 92 | 59% |
| 3 | 0.01 M | 83 | 86% |
| 4 | 0.033 M | 84 | 84% |
| 5 | 0.04 M | 85 | 81% |
| 6 | 0.1 M | 83 | 81% |
| 7 | 0.4 M | 89 | 78% |
| 8 | 1 M | 79 | 72% |

a) Substrate **5b** (0.035 mmol), Pd[(Cinnamyl)Cp] (**30**, 10 mol%), **6a** (11 mol%) and MTBE (X M) at 25 °C. Isolated yield after flash chromatography is given, the *ee* are measured with chiral HPLC.

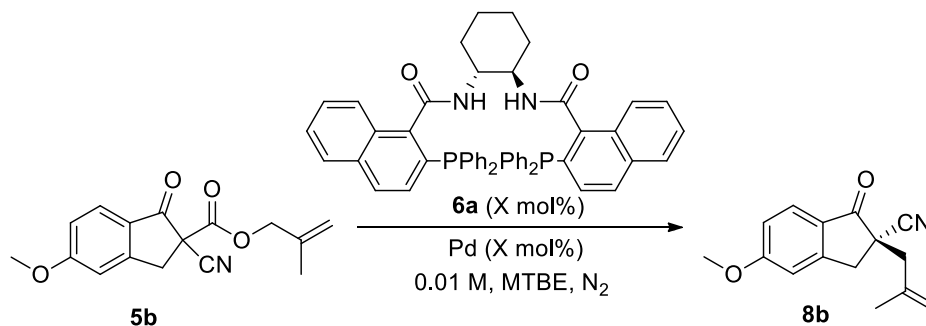
Supplementary Table S14 | Screening of Catalyst/Ligand Loading



| Entry | Catalyst/Ligand | Yield% | <i>ee</i> % ^a |
|----------|-----------------|-------------------|--------------------------|
| 1 | 2.5/2.75% | n.r. ^b | - |
| 2 | 5/5.5% | n.r. ^b | 86% |
| 3 | 5/10% | 91 | 83% |
| 4 | 5/20% | 86 | 85% |
| 5 | 10/11% | 89 | 86% |

a) Substrate **11b** (0.035 mmol), Pd[(Cinnamyl)Cp] (**34**, X mol%), L (X mol%) and MTBE (0.01 M) at 25 °C. Isolated yield after flash chromatography is given, the *ee* are measured with chiral HPLC. b) No complete conversion after 48 hours.

Supplementary Table S15 | Screening of the Palladium Source

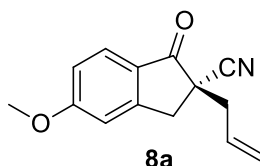


| Entry | Palladium Source | Yield% | <i>ee</i> % ^a |
|-------|---|--------|--------------------------|
| 1 | Pd(dba) ₂ 10% - Dach Naphtyl 11 % | 87 | 77% |
| 2 | Pd ₂ (dba) ₃ 5% - Dach | 87 | 88% |

| | | | |
|----------|---|-----------|------------|
| | Naphtyl 11 % | | |
| 3 | Pd₂(dba)₃ 2.5% - Dach Naphtyl 5.5% | 87 | 89% |

a) Substrate **5b** (0.035 mmol), Pd source (X mol%), L **6a** (X mol%) and MTBE (0.01 M) at 25 °C. Isolated yield after flash chromatography is given, the *ee* are measured with chiral HPLC.

(S)-2-Allyl-5-methoxy-1-oxo-2,3-dihydro-1H-indene-2-carbonitrile (8a)



Following general procedure **GP5**, but using PdCynnamylCp (**30**) (0.006 g, 0.02 mmol, 5 mol%) as catalyst, starting from substrate **5a** (0.054 g, 0.20 mmol), (*S*)-5-methoxy-2-(2-methylallyl)-1-oxo-2,3-dihydro-1H-indene-2-carbonitrile (**8a**) (0.041 g, 0.18 mmol, 91 % yield, 79% *ee*) was obtained as an yellow oil.

R_F 0.5 (Pentane: Ethyl acetate 4:1).

Chiral HPLC conditions: *ee*: 79%; Chiralcel IA 95:5 Hexane/*i*PrOH, 1 mL/min, 30 min. *t_{R1}* = 19.1 min and *t_{R2}* = 23.4 min. λ = 280 cm⁻¹.

¹H NMR (400 MHz, Chloroform-*d*) δ 7.76 (d, *J* = 8.6 Hz, 1H, Ar*H*), 6.98 (dd, *J* = 8.7, 2.2 Hz, 1H, Ar*H*), 6.92 – 6.82 (m, 1H, Ar*H*), 5.81 (m, 1H, CHCH₂), 5.35 – 5.16 (m, 2H, CCH₂), 3.91 (s, 3H, OMe), 3.52 (d, *J* = 17.4 Hz, 1H, CH₂), 3.29 (d, *J* = 17.4 Hz, 1H, CH₂), 2.82 (dd, *J* = 13.9, 6.7 Hz, 1H, CH₂CH), 2.47 (dd, *J* = 13.9, 7.6 Hz, 1H, CH₂CH).

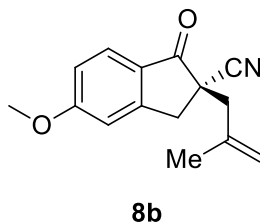
¹³C NMR (101.00 MHz, Chloroform-*d*) δ 195.5, 166.8, 153.9, 130.9, 127.4, 126.5, 121.2, 119.8, 116.9, 109.8, 56.0, 47.5, 40.8, 37.2.

IR ν_{max} 3084 (w), 2945 (w), 2929 (w), 2845 (w), 2239 (w), 1718 (s), 1601 (s), 1492 (w), 1437 (w), 1268 (s), 1150 (w), 1093 (m), 1025 (m).

HRMS (ESI) calcd for C₁₄H₁₄NO₂⁺ [M+H]⁺ 228.1019; found 228.1022.

[α]_D^{25.0} +50.4 (c = 11.0, CHCl₃).

(S)-5-Methoxy-2-(2-methylallyl)-1-oxo-2,3-dihydro-1H-indene-2-carbonitrile (8b)



Following general procedure **GP5**, starting from substrate **5b** (0.057 g, 0.20 mmol), (*S*)-5-methoxy-2-(2-methylallyl)-1-oxo-2,3-dihydro-1*H*-indene-2-carbonitrile (**8b**) (0.044 g, 0.18 mmol, 92% yield, 89% *ee*) was obtained as an orange resin.

R_F 0.4 (Pentane: Ethyl acetate 4:1).

Chiral HPLC conditions: *ee*: 89%; Chiralcel IA 95:5 Hexane/*i*PrOH, 1 mL/min, 30 min. *t_{R1}* = 16.4 min and *t_{R2}* = 22.8 min. λ = 254 cm⁻¹.

¹H NMR (400 MHz, Chloroform-*d*) δ 7.75 (d, *J* = 8.6 Hz, 1H, Ar*H*), 6.98 (dd, *J* = 8.6, 2.2 Hz, 1H, Ar*H*), 6.88 (s, 1H, Ar*H*), 4.99 (s, 1H, CCH₂), 4.88 (s, 1H, CCH₂), 3.91 (s, 3H, OMe), 3.53 (d, *J* = 17.5 Hz, 1H, CH₂), 3.37 (d, *J* = 17.5 Hz, 1H, CH₂), 2.84 (d, *J* = 14.5 Hz, 1H, CH₂CMe), 2.38 (d, *J* = 14.5 Hz, 1H, CH₂CMe), 1.84 (d, *J* = 1.5 Hz, 3H, CH₃).

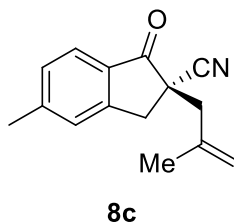
¹³C NMR (101.00 MHz, Chloroform-*d*) δ 195.8, 166.8, 154.1, 139.9, 127.5, 126.1, 120.4, 116.9, 116.6, 109.8, 56.0, 46.9, 43.7, 37.3, 23.3.

IR ν_{max} 3082 (w), 2945 (w), 2922 (w), 2844 (w), 2238 (w), 1715 (s), 1599 (s), 1492 (w), 1265 (s), 1089 (m), 1023 (m), 909 (m).

HRMS (ESI) calcd for C₁₅H₁₆NO₂⁺ [M+H]⁺ 242.1176; found 242.1169.

[α]_D^{25.0} +61.6 (*c* = 3.1, CHCl₃).

(*S*)-5-Methyl-2-(2-methylallyl)-1-oxo-2,3-dihydro-1*H*-indene-2-carbonitrile (**8c**)



Following general procedure **GP5**, starting from substrate **5c** (0.054 g, 0.20 mmol), (*S*)-5-methyl-2-(2-methylallyl)-1-oxo-2,3-dihydro-1*H*-indene-2-carbonitrile (**8c**) (0.044 g, 0.19 mmol, 98% yield, 82% *ee*) was obtained as white crystal.

R_F 0.35 (Pentane:Ethyl acetate 4:1).

Mp 42-45 °C.

Chiral HPLC conditions: *ee*: 82%; Chiralcel IA 95:5 Hexane/*i*PrOH, 1 mL/min, 30 min. *t_{R1}* = 10.0 min and *t_{R2}* = 15.4 min. λ = 254 cm⁻¹.

¹H NMR (400 MHz, Chloroform-*d*) δ 7.73 (d, *J* = 8.2 Hz, 1H, Ar*H*), 7.26 (m, 2H, Ar*H*²¹), 5.00 (s, 1H, CCH₂), 4.87 (s, 1H, CCH₂), 3.55 (d, *J* = 17.4 Hz, 1H, CH₂), 3.38 (d, *J* = 17.4 Hz, 1H, CH₂), 2.84 (d, *J* = 14.4 Hz, 1H, CH₂CMe), 2.47 (s, 3H, ArCH₃), 2.43 – 2.29 (m, 1H, CH₂CMe), 1.85 (d, *J* = 1.1 Hz, 3H, CH₃).

²¹ CDCl₃ peak overlaps with the aromatic protons of the molecule.

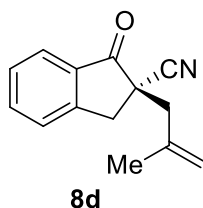
^{13}C NMR (101.00 MHz, Chloroform-*d*) δ 197.3, 151.5, 148.3, 139.9, 130.9, 130.1, 127.1, 125.6, 120.3, 116.7, 46.9, 43.7, 37.2, 23.3, 22.4.

IR ν_{max} 3079 (w), 2975 (w), 2924 (w), 2857 (w), 2238 (w), 1720 (s), 1609 (s), 1435 (w), 1275 (m), 1120 (w), 909 (m)

HRMS (ESI) calcd for $\text{C}_{15}\text{H}_{16}\text{NO}^+$ $[\text{M}+\text{H}]^+$ 226.1226; found 226.1220.

$[\alpha]_{\text{D}}^{25.0}$ +52.2 ($c = 3.6$, CHCl_3).

(S)-2-(2-Methylallyl)-1-oxo-2,3-dihydro-1*H*-indene-2-carbonitrile (8d)



Following general procedure **GP5**, starting from substrate **5d** (0.051 g, 0.20 mmol), (S)-2-(2-methylallyl)-1-oxo-2,3-dihydro-1*H*-indene-2-carbonitrile (**8d**) (0.041 g, 0.19 mmol, 96% yield, 85% *ee*) was obtained as an orange oil.

R_F 0.25 (Pentane: Ethyl acetate 4:1).

Chiral HPLC conditions: *ee*: 85%; Chiralcel IA 95:5 Hexane/*i*PrOH, 1 mL/min, 30 min. $t_{\text{R1}} = 8.5$ min and $t_{\text{R2}} = 11.3$ min. $\lambda = 254$ nm.

^1H NMR (400 MHz, Chloroform-*d*) 7.84 (d, $J = 7.7$ Hz, 1H, Ar*H*), 7.77 – 7.66 (m, 1H, Ar*H*), 7.57 – 7.41 (m, 2H, Ar*H*), 5.01 (s, 1H, CCH_2), 4.89 (s, 1H, CCH_2), 3.61 (d, $J = 17.4$ Hz, 1H, CH_2), 3.44 (d, $J = 17.4$ Hz, 1H, CH_2), 2.85 (d, $J = 14.5$, 1H, CH_2CMe), 2.39 (d, $J = 14.5$, 1H, CH_2CMe), 1.85 (s, 3H, CH_3).

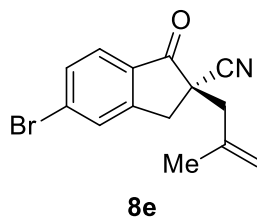
^{13}C NMR (101.00 MHz, Chloroform-*d*) δ 197.8, 151.0, 139.8, 136.6, 133.2, 128.8, 126.8, 125.8, 120.1, 116.8, 46.7, 43.7, 37.4, 23.3

IR ν_{max} 3076 (w), 2974 (w), 2923 (w), 2856 (w), 2239 (w), 1731 (s), 1612 (w), 1466 (w), 1436 (w), 1301 (w), 1214 (w), 1016 (w), 912 (w)

HRMS (ESI) calcd for $\text{C}_{14}\text{H}_{14}\text{NO}^+$ $[\text{M}+\text{H}]^+$ 212.1070; found 212.1063.

$[\alpha]_{\text{D}}^{25.0}$ +9.3 ($c = 3.1$, CHCl_3).

(S)-5-Bromo-2-(2-methylallyl)-1-oxo-2,3-dihydro-1H-indene-2-carbonitrile (8e)



Following general procedure **GP5**, starting from substrate **5e** (0.067 mg, 0.20 mmol), (*S*)-5-bromo-2-(2-methylallyl)-1-oxo-2,3-dihydro-1*H*-indene-2-carbonitrile (**8e**) (0.052 mg, 0.18 mmol, 90% yield, 78% *ee*) was obtained as an orange oil.

R_F 0.75 (Pentane:Ethyl acetate 9:1).

Chiral HPLC conditions: *ee*: 78%; Chiralcel IA 95:5 Hexane/*i*PrOH, 1 mL/min, 30 min. t_{R1} = 10.0 min and t_{R2} = 16.9 min. λ = 280 cm⁻¹.

¹H NMR (400 MHz, Chloroform-*d*) δ 7.75 – 7.66 (m, 2H, Ar*H*), 7.62 (d, *J* = 8.2 Hz, 1H, Ar*H*), 5.01 (s, 1H, CCH₂), 4.87 (s, 1H, CCH₂), 3.58 (d, *J* = 17.8 Hz, 1H, CH₂), 3.42 (d, *J* = 17.6 Hz, 1H, CH₂), 2.84 (d, *J* = 14.4 Hz, 1H, CH₂CMe), 2.40 (d, *J* = 14.4 Hz, 1H, CH₂CMe), 1.84 (s, 3H, CH₃).

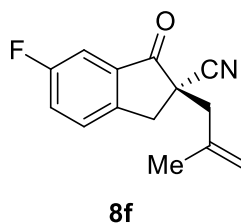
¹³C NMR (101.00 MHz, Chloroform-*d*) δ 196.6, 152.4, 139.5, 132.6, 132.3, 132.1, 130.1, 126.9, 119.6, 117.1, 46.8, 43.7, 36.9, 23.3.

IR ν_{\max} 3081 (w), 2925 (w), 2852 (w), 2239 (w), 1729 (s), 1596 (s), 1578 (m), 1416 (w), 1318 (m), 1265 (m), 1209 (m), 1061 (m), 912 (m).

HRMS (ESI) calcd for C₁₄H₁₃⁷⁹BrNO⁺ [M+H]⁺ 290.0175; found 290.0174.

[α]_D^{25.0} +26.9 (c = 2.3, CHCl₃).

(S)-6-Fluoro-2-(2-methylallyl)-1-oxo-2,3-dihydro-1H-indene-2-carbonitrile (8f)



Following general procedure **GP5**, starting from substrate **5f** (0.055 g, 0.20 mmol), (*S*)-6-fluoro-2-(2-methylallyl)-1-oxo-2,3-dihydro-1*H*-indene-2-carbonitrile (**8f**) (0.037 g, 0.16 mmol, 81% yield, 78% *ee*) was obtained as an orange oil.

R_F 0.8 (Pentane:Ethyl acetate 4:1).

Chiral HPLC conditions: *ee*: 78%; Chiralcel IA 95:5 Hexane/*i*PrOH, 1 mL/min, 30 min. t_{R1} = 8.2 min and t_{R2} = 9.6 min. λ = 280 cm⁻¹.

¹H NMR (400 MHz, Chloroform-*d*) δ 7.54 – 7.35 (m, 3H, ArH), 5.01 (s, 1H, CCH₂), 4.87 (s, 1H, CCH₂), 3.57 (d, *J* = 17.5 Hz, 1H, CH₂), 3.40 (d, *J* = 17.5 Hz, 1H, CH₂), 2.83 (d, *J* = 14.5 Hz, 1H, CH₂CMe), 2.41 (d, *J* = 14.5 Hz, 1H, CH₂CMe), 1.84 (s, 3H, CH₃).

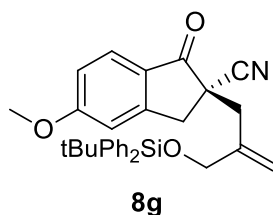
¹³C NMR (101.00 MHz, Chloroform-*d*) δ 196.8, 162.8 (d, *J* = 250.5 Hz), 146.3 (d, *J* = 2.0 Hz), 139.4, 134.9, 134.8 (d, *J* = 7.8 Hz), 128.2 (d, *J* = 8.1 Hz), 124.4 (d, *J* = 23.8 Hz), 119.6, 116.9, 111.3 (d, *J* = 22.4 Hz), 47.5, 43.5, 36.7, 23.2.

IR ν_{max} 3730 (w), 3625 (w), 3076 (w), 2926 (w), 2856 (w), 2241 (w), 1732 (s), 1614 (w), 1490 (m), 1442 (m), 1268 (m), 908 (w).

HRMS (ESI) calcd for C₁₄H₁₃FNO⁺ [M+H]⁺ 230.0976; found 230.0975.

[α]_D^{25.0} +21.5 (c = 3.6, CHCl₃).

(*R*)-2-(2-(((tert-butyldiphenylsilyl)oxy)methyl)allyl)-5-methoxy-1-oxo-2,3-dihydro-1*H*-indene-2-carbonitrile (8g)



Following general procedure **GP5**, starting from substrate **5g** (0.108 g, 0.200 mmol), (*R*)-2-(2-(((tert-butyldiphenylsilyl)oxy)methyl)allyl)-5-methoxy-1-oxo-2,3-dihydro-1*H*-indene-2-carbonitrile (**8g**) (0.046 g, 0.090 mmol, 46% yield, 93% *ee*) was obtained as white oil after 48 hours of reaction.

R_F 0.55 (Pentane:Ethyl acetate 4:1).

Chiral HPLC conditions: *ee*: 93%; Chiralcel IC 95:5 Hexane/*i*PrOH, 1 mL/min, 25 min. *t*_{R1} = 8.2 min and *t*_{R2} = 9.6 min. λ = 254 cm⁻¹.

¹H NMR (400 MHz, Chloroform-*d*) δ 7.73 (d, *J* = 8.6 Hz, 1H, ArH), 7.68 – 7.60 (m, 4H, ArH), 7.47 – 7.33 (m, 6H, ArH), 6.96 (dd, *J* = 8.6, 2.2 Hz, 1H, ArH), 6.80 (d, *J* = 2.2 Hz, 1H, ArH), 5.38 (s, 1H, CCH₂), 5.16 (s, 1H, CCH₂), 4.21 (d, *J* = 14.3 Hz, 1H, CH₂O), 4.10 (d, *J* = 14.1 Hz, 1H, CH₂O), 3.90 (s, 3H, OMe), 3.46 (d, *J* = 17.5 Hz, 1H, CH₂CCH₂), 3.35 (d, *J* = 17.5 Hz, 1H, CH₂CCH₂), 2.86 (d, *J* = 14.8 Hz, 1H, CH₂), 2.42 (d, *J* = 14.8 Hz, 1H, CH₂), 1.05 (s, 9H, SiC(CH₃)₃).

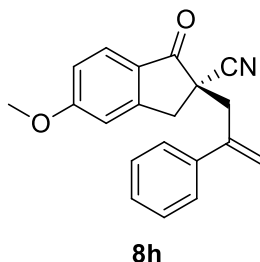
¹³C NMR (101.00 MHz, Chloroform-*d*) δ 195.7, 166.8, 154.2, 142.2, 135.6, 133.4, 133.3, 129.9, 127.9, 127.5, 126.2, 120.1, 116.9, 115.2, 109.8, 77.4, 66.7, 56.0, 47.4, 38.5, 37.6, 27.0, 19.4.²²

IR ν_{max} 3072 (w), 2958 (w), 2932 (w), 2857 (w), 2238 (w), 1718 (s), 1601 (s), 1429 (m), 1267 (s), 1113 (s), 912 (m), 827 (m)

HRMS (ESI) calcd for C₃₁H₃₃NNaO₃Si⁺ [M+Na]⁺ 518.2122; found 518.2138.

[α]_D^{25.0} +30.6 (c = 1.1, CHCl₃).

(*S*)-5-Methoxy-1-oxo-2-(2-phenylallyl)-2,3-dihydro-1*H*-indene-2-carbonitrile (8h)



Following general procedure **GP5**, starting from substrate **5h** (0.070 g, 0.20 mmol), (*S*)-5-methoxy-1-oxo-2-(2-phenylallyl)-2,3-dihydro-1*H*-indene-2-carbonitrile (**8h**) (0.052 g, 0.17 mmol, 86% yield, 88% *ee*) was obtained as yellow oil after 48 hours of reaction.

R_F 0.55 (Pentane:Ethyl acetate 4:1).

Chiral HPLC conditions: *ee*: 88%; Chiralcel IA 95:5 Hexane/*i*PrOH, 1 mL/min, 35 min. t_{R1} = 23.7 min and t_{R2} = 30.0 min. λ = 254 cm⁻¹.

¹H NMR (400 MHz, Chloroform-*d*) δ 7.63 (d, *J* = 8.6 Hz, 1H, Ar*H*), 7.31 – 7.20 (m, 5H, Ar*H*²³), 6.92 (dd, *J* = 8.7, 2.2 Hz, 1H, Ar*H*), 6.72 (d, *J* = 2.2 Hz, 1H, Ar*H*), 5.39 (s, 1H, CCH₂), 5.32 (s, 1H, CCH₂), 3.87 (s, 3H, OMe), 3.39 – 3.26 (m, 2H, CH₂CPh + CH₂), 3.17 (d, *J* = 17.5 Hz, 1H, CH₂CPh), 2.98 (dd, *J* = 14.3, 1.0 Hz, 1H, CH₂).

¹³C NMR (101.00 MHz, Chloroform-*d*) δ 195.6, 166.7, 154.2, 143.1, 140.7, 135.7, 128.6, 128.2, 127.3, 126.7, 119.9, 119.1, 116.9, 109.5, 56.0, 48.1, 41.3, 37.2.

IR 3057 (w), 3022 (w), 2930 (w), 2851 (w), 2239 (w), 1719 (s), 1601 (s), 1493 (w), 1447 (w), 1268 (s), 1092 (m), 1026 (w), 914 (w).

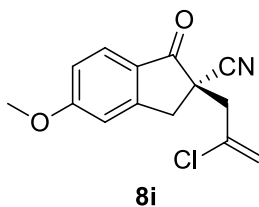
HRMS (ESI) calcd for C₂₀H₁₈NO₂⁺ [M+H]⁺ 304.1332; found 304.1321.

[α]_D^{25.0} +32.0 (c = 1.2, CHCl₃).

²² Not all carbons resolved in the spectra.

²³ CDCl₃ peak overlaps with the aromatic protons of the molecule

(R)-2-(2-Chloroallyl)-5-methoxy-1-oxo-2,3-dihydro-1H-indene-2-carbonitrile (8i)



Following general procedure **GP5**, starting from substrate **5i** (0.061 g, 0.20 mmol), (*R*)-5-methoxy-1-oxo-2-(2-phenylallyl)-2,3-dihydro-1*H*-indene-2-carbonitrile (**8i**) (0.039 g, 0.15 mmol, 75% yield, 92% *ee*) was obtained as yellow oil after 6 hours of reaction.

R_F 0.30 (Pentane:Ethyl acetate 4:1).

Chiral HPLC conditions: *ee*: 92%; Chiralcel IA 95:5 Hexane/*i*PrOH, 1 mL/min, 35 min. *t_{R1}* = 20.6 min and *t_{R2}* = 33.4 min. λ = 254 cm⁻¹.

¹H NMR (400 MHz, Chloroform-*d*) δ 7.77 (d, *J* = 8.6 Hz, 1H, Ar*H*), 6.99 (dd, *J* = 8.6, 2.3 Hz, 1H, Ar*H*), 6.95 – 6.87 (m, 1H, Ar*H*), 5.45 (s, 2H, CCH₂), 3.92 (s, 3H, OMe), 3.63 (s, 2H, CH₂CCl), 3.21 (d, *J* = 14.8 Hz, 1H, CH₂), 2.71 (d, *J* = 14.8 Hz, 1H, CH₂).

¹³C NMR (101.00 MHz, Chloroform-*d*) δ 194.6, 167.0, 154.3, 135.9, 127.6, 126.1, 119.2, 118.5, 117.2, 109.8, 56.1, 47.6, 44.3, 37.6.

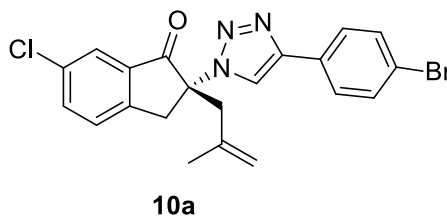
IR ν_{max} 2923 (w), 2849 (w), 2239 (w), 1717 (s), 1599 (s), 1493 (w), 1341 (w), 1303 (m), 1263 (s), 1149 (w), 1092 (m), 1022 (m), 908 (w).

HRMS (ESI) calcd for C₁₄H₁₃ClNO₂⁺ [M+H]⁺ 262.0629; found 262.0621.

[α]_D^{25.0} +98.0 (*c* = 1.6, CHCl₃).

6. Product Modifications

(R)-2-(4-(4-Bromophenyl)-1*H*-1,2,3-triazol-1-yl)-6-chloro-2-(2-methylallyl)-2,3-dihydro-1*H*-inden-1-one (10a)



Following a reported procedure,²⁴ in an open flask (*R*)-2-azido-6-chloro-2-(2-methylallyl)-2,3-dihydro-1*H*-inden-1-one (**7g**) (0.020 g, 0.075 mmol), 1-bromo-4-ethynylbenzene **9** (0.014 g, 0.080 mmol, 1.2 equiv) and TBTA (0.4 mg, 0.7 μ mol, 0.01 equiv) were dissolved in ^tBuOH (0.3

²⁴ Q.H. Deng, T. Bleith, H. Wadepohl, and L.H. Gade, *J. Am. Chem. Soc.* **2013**, *135*, 5356.

mL, then sodium ascorbate (0.006 g, 0.03 mmol, 0.4 equiv) and copper sulphate pentahydrate (0.004 g, 0.02 mmol, 0.2 equiv) dissolved in H₂O (0.15 mL), were added under vigorous stirring and the reaction monitored by TLC (4:1 Pentane:EtOAc). Upon consumption of the starting material the reaction mixture was diluted with water (5 mL) and extracted with DCM (3x5 mL). The combined organic layers were dried over MgSO₄ and the solvent removed *in vacuo*. The crude was then purified with flash chromatography (4:1 Pentane:EtOAc) to afford (*R*)-2-(4-(4-bromophenyl)-1*H*-1,2,3-triazol-1-yl)-6-chloro-2-(2-methylallyl)-2,3-dihydro-1*H*-inden-1-one (**10a**) as a white oil (0.031 g, 0.070 mmol, 94% yield)

Rf: 0.31 (Pentane:Ethyl Acetate 4:1).

¹H NMR (400 MHz, Chloroform-*d*) δ 8.34 (s, 1H, Ar*H*), 7.78 (d, *J* = 2.0 Hz, 1H, Ar*H*), 7.77 – 7.70 (m, 2H, Ar*H*), 7.67 (dd, *J* = 8.2, 2.1 Hz, 1H, Ar*H*), 7.62 – 7.45 (m, 3H, Ar*H*), 4.89 (s, 1H, CCH₂), 4.69 (s, 1H, CCH₂), 4.63 (d, *J* = 18.0 Hz, 1H, CH₂CMe), 3.78 (d, *J* = 18.0 Hz, 1H, CH₂CMe), 2.98 (d, *J* = 14.5 Hz, 1H, CH₂), 2.80 (dd, *J* = 14.6, 1.1 Hz, 1H, CH₂), 1.49 (s, 3H, CH₃).

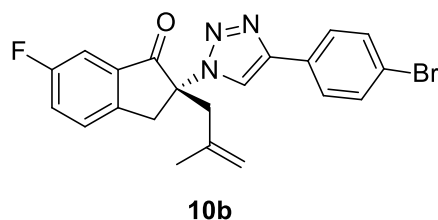
¹³C NMR (101.00 MHz, Chloroform-*d*) δ 199.5, 150.2, 147.2, 138.7, 136.9, 135.0, 134.7, 132.1, 129.6, 128.0, 127.4, 125.2, 122.3, 119.1, 117.6, 71.1, 46.3, 36.5, 23.3.

IR ν_{max} 3148 (w), 3080 (w), 2921 (w), 1726 (s), 1477 (s), 1428 (s), 1256 (m), 1200 (m), 1184 (m), 1070 (m), 1010 (s)

HRMS (ESI) calcd for C₂₁H₁₈⁷⁹BrClN₃O⁺ [M+H]⁺ 442.0316; found 442.0308.

[α]_D^{25.0} +53.2 (c = 0.2, CHCl₃).

(*R*)-2-(4-(4-Bromophenyl)-1*H*-1,2,3-triazol-1-yl)-6-fluoro-2-(2-methylallyl)-2,3-dihydro-1*H*-inden-1-one (10b)



Following a reported procedure,²¹ in an open flask (*R*)-2-azido-6-fluoro-2-(2-methylallyl)-2,3-dihydro-1*H*-inden-1-one (**7i**) (0.017 g, 0.070 mmol), 1-bromo-4-ethynylbenzene **9** (0.013 g, 0.071 mmol, 1.2 equiv) and TBTA (0.4 mg, 0.7 μ mol, 0.01 equiv) were dissolved in ^tBuOH (0.3 mL), then sodium ascorbate (0.006 g, 0.03 mmol, 0.4 equiv) and copper sulphate pentahydrate (0.003 g, 0.01 mmol, 0.2 equiv) dissolved in H₂O (0.15 mL), were added under vigorous stirring and the reaction monitored by TLC (4:1 Pentane:EtOAc). Upon consumption of the starting material the reaction mixture was diluted with water (5 mL) and extracted with DCM (3x5 mL). The combined organic layers were dried over MgSO₄ and the solvent removed *in vacuo*. The crude was then purified with flash chromatography (4:1 Pentane:EtOAc) to afford (*R*)-2-(4-(4-bromophenyl)-1*H*-1,2,3-triazol-1-yl)-6-fluoro-2-(2-methylallyl)-2,3-dihydro-1*H*-inden-1-one (**10b**) as a white oil (0.029 g, 0.070 mmol, 96% yield)

Rf: 0.35 (4:1 Pentane:Ethyl Acetate 4:1).

¹H NMR (400 MHz, Chloroform-*d*) δ 8.34 (s, 1H, ArH), 7.73 (d, *J* = 8.5 Hz, 2H, ArH), 7.55 (m, 3H, ArH), 7.50 – 7.39 (m, 2H, ArH), 4.89 (s, 1H, CCH₂), 4.70 (s, 1H, CCH₂), 4.63 (d, *J* = 17.7 Hz, 1H, CCH₂), 3.78 (d, *J* = 17.7 Hz, 1H, CCH₂), 2.99 (d, *J* = 14.5 Hz, 1H, CH₂), 2.82 (d, *J* = 14.5 Hz, 1H, CH₂), 1.49 (s, 3H, CH₃).

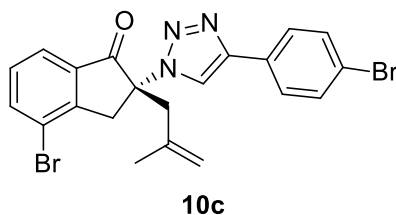
¹³C NMR (101.00 MHz, Chloroform-*d*) δ 199.9 (d, *J* = 3.0 Hz), 162.8 (d, *J* = 250.0 Hz), 147.6 (d, *J* = 2.2 Hz), 147.2, 138.7, 134.9 (d, *J* = 7.7 Hz), 132.1, 129.6, 128.4 (d, *J* = 7.9 Hz), 127.4, 124.8 (d, *J* = 23.8 Hz), 122.3, 119.1, 117.6, 111.2 (d, *J* = 22.2 Hz), 71.4, 46.3, 36.4, 23.3.

IR ν_{max} 3149 (w), 3076 (w), 2922 (w), 2854 (w), 1726 (s), 1488 (s), 1441 (m), 1267 (s), 1070 (m), 1011 (m).

HRMS (ESI) calcd for C₂₁H₁₈⁷⁹BrFN₃O⁺ [M+H]⁺ 426.0612; found 426.0608.

[α]_D^{25.0} +15.0 (c = 0.1 g/mL, CHCl₃).

(*R*)-4-Bromo-2-(4-(4-bromophenyl)-1H-1,2,3-triazol-1-yl)-2-(2-methylallyl)-2,3-dihydro-1H-inden-1-one (10c)



Following a reported procedure,²¹ in an open flask, (*R*)-2-azido-4-bromo-2-(2-methylallyl)-2,3-dihydro-1H-inden-1-one (**7j**) (0.043 g, 0.14 mmol), 1-bromo-4-ethynylbenzene **9** (0.025 g, 0.14 mmol, 1.2 equiv) and TBTA (0.70 mg, 1.4 μ mol, 0.01 equiv) were dissolved in ^tBuOH (0.6 mL, then sodium ascorbate (0.011 g, 0.060 mmol, 0.4 equiv) and copper sulphate pentahydrate (0.007 g, 0.03 mmol, 0.2 equiv) dissolved in H₂O (0.3 mL, were added under vigorous stirring and the reaction monitored by TLC (4:1 Pentane:EtOAc). Upon consumption of the starting material the reaction mixture was diluted with water (5 mL) and extracted with DCM (3x5 mL). The combined organic layers were dried over MgSO₄ and the solvent removed *in vacuo*. The crude was then purified with flash chromatography (4:1 Pentane:EtOAc) to afford (*R*)-4-bromo-2-(4-(4-bromophenyl)-1H-1,2,3-triazol-1-yl)-2-(2-methylallyl)-2,3-dihydro-1H-inden-1-one (**10c**) as an orange oil (0.065 g, 0.13 mmol, 96% yield).

Rf: 0.35 (4:1 Pentane:Ethyl Acetate 4:1).

¹H NMR (400 MHz, Chloroform-*d*) δ 8.33 (s, 1H, ArH), 7.87 (dd, *J* = 7.8, 1.0 Hz, 1H, ArH), 7.82 – 7.68 (m, 3H, ArH), 7.54 (d, *J* = 8.5 Hz, 2H, ArH), 7.41 – 7.31 (m, 1H, ArH), 4.90 (s, 1H, CCH₂), 4.72 (s, 1H, CCH₂), 4.58 (d, *J* = 18.3 Hz, 1H, CH₂CMe), 3.75 (d, *J* = 18.3 Hz, 1H, CH₂CMe), 3.08 – 2.93 (m, 1H, CH₂), 2.86 – 2.75 (m, 1H, CH₂), 1.50 (dd, *J* = 1.5, 0.8 Hz, 3H, CH₃).

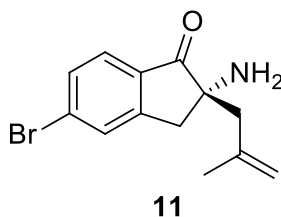
¹³C NMR (101.00 MHz, Chloroform-*d*) δ 200.0, 171.2, 151.7, 147.1, 139.4, 138.4, 135.0, 132.0, 130.1, 129.5, 127.3, 124.2, 122.1, 119.0, 117.6, 70.5, 60.4, 46.0, 38.0, 23.3, 21.1, 14.2.

IR ν_{\max} 3157 (w), 3078 (w), 2975 (w), 1727 (s), 1597 (m), 1459 (m), 1266 (s), 1126 (m), 1070 (s), 1010 (s).

HRMS (ESI) calcd for C₂₁H₁₈⁷⁹Br₂N₃O⁺ [M+H]⁺ 485.9811; found 442.9795.

[α]_D^{25.0} +40.2 (c = 0.2, CHCl₃).

(*R*)-2-Amino-5-bromo-2-(2-methylallyl)-2,3-dihydro-1*H*-inden-1-one (11)



Following a reported procedure,²⁵ 2-azido-5-bromo-2-(2-methylallyl)-2,3-dihydro-1*H*-inden-1-one (**7e**) (0.050 mg, 0.16 mmol) was dissolved in 3 mL of anhydrous THF under N₂ in an 10 mL flask. Then triphenylphosphine (0.129 mg, 0.490 mmol, 3 equiv) was added under vigorous stirring at 0 °C. The clear solution was monitored by TLC (Pentane:EtOAc 2:1) and left stirring until consumption of the starting material. Then the reaction was quenched with water (3 mL) and the water phase was extracted three times with EtOAc (3x5 mL). The crude was then purified with flash chromatography (2:1 Pentane:EtOAc) to afford (*R*)-2-amino-5-bromo-2-(2-methylallyl)-2,3-dihydro-1*H*-inden-1-one (**11**) (0.024 g, 0.086 mmol, 53% yield) as a yellow oil.

Rf: 0.40 (Pentane:Ethyl Acetate 2:1).

¹H NMR (400 MHz, Chloroform-*d*) δ 7.70 – 7.59 (m, 2H, Ar*H*), 7.58 – 7.49 (m, 1H, Ar*H*), 4.87 (s, 1H, CCH₂), 4.75 (s, 1H, CCH₂), 3.40 (d, *J* = 17.6 Hz, 1H, CH₂), 2.92 (d, *J* = 17.6 Hz, 1H, CH₂), 2.41 (s, 2H, CH₂CMe), 1.71 – 1.64 (m, 5H, NH₂+CH₃).

¹³C NMR (101.00 MHz, Chloroform-*d*) δ 208.1, 153.5, 141.2, 133.6, 131.6, 131.0, 130.1, 126.1, 116.0, 62.9, 46.7, 40.3, 24.3.

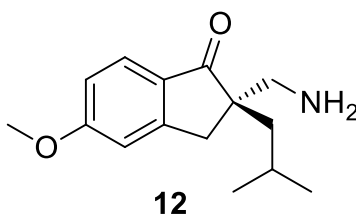
IR ν_{\max} 3072 (w), 2926 (w), 2850 (w), 2078 (w), 1719 (s), 1596 (s), 1574 (m), 1416 (w), 1317 (m), 1205 (m), 1060 (w), 933 (m), 900 (m).

HRMS (ESI) calcd for C₁₃H₁₄⁷⁹BrNNaO⁺ [M+Na]⁺ 302.0151; found 302.0153.

[α]_D^{25.0} +4.67 (c = 2.4, CHCl₃).

²⁵ R. Rossi Paccani, D. Donati, S. Fusi, L. Latterini, G. Farina, V. Zanirato, M. Olivucci, *J. Org. Chem.* **2012**, 77, 1738.

(S)-2-(Aminomethyl)-2-isobutyl-5-methoxy-2,3-dihydro-1H-inden-1-one (12)



Following a reported procedure,²⁶ substrate **8b** (0.040 g, 0.16 mmol) was dissolved in anhydrous MeOH (0.6 mL) and CHCl₃ (0.9 mL). Then PtO₂ (15 mg, 0.066 mmol, 0.4 equiv.) was added in one portion and the resulting suspension bubbled with hydrogen for one hour. Then the reaction was left stirring under hydrogen atmosphere for 36 hours. The suspension was then filtrated on a celite pad that was washed with MeOH (3x5 mL). Flash chromatography in pure EtOAc afforded (S)-2-(aminomethyl)-2-isobutyl-5-methoxy-2,3-dihydro-1H-inden-1-one (**12**) (0.017 g, 0.068 mmol, 41% yield) as a light yellow oil.

Rf: 0.2 (Ethyl Acetate 100%).

¹H NMR (400 MHz, Chloroform-*d*) δ 7.68 (d, *J* = 9.2 Hz, 1H, Ar*H*), 6.95 – 6.86 (m, 2H, Ar*H*), 3.89 (s, 3H, OMe), 3.19 – 2.93 (m, 3H, CH₂), 2.73 (d, *J* = 12.9 Hz, 1H, CH₂), 2.12 (br s, 2H, NH₂), 1.64 – 1.63 (m, 2H, CH₂), 1.25 (m, 1H, CH), 0.89 (d, *J* = 6.4 Hz, 3H, CH₃), 0.75 (d, *J* = 6.4 Hz, 3H, CH₃).

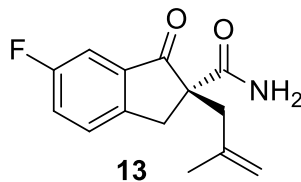
¹³C NMR (101.00 MHz, Chloroform-*d*) δ 209.0, 165.8, 156.6, 130.2, 125.8, 115.8, 109.7, 55.8, 54.2, 49.4, 43.3, 36.6, 25.2, 25.0, 23.8.

IR ν_{max} 3441 (w), 2940 (w), 2886 (m), 1697 (m), 1599 (s), 1492 (w), 1440 (w), 1262 (s), 1092 (w), 1027 (w), 844 (w)

HRMS (ESI) calcd for C₁₅H₂₂NO₂⁺ [M+H]⁺ 248.1645; found 248.1645.

[α]_D^{25.0} +1.1 (*c* = 1.7, CHCl₃).

(R)-6-Fluoro-2-(2-methylallyl)-1-oxo-2,3-dihydro-1H-indene-2-carboxamide (13)



Following a reported procedure,²⁷ a mixture of (S)-6-fluoro-2-(2-methylallyl)-1-oxo-2,3-dihydro-1H-indene-2-carbonitrile (**8f**) (0.050 g, 0.22 mmol), (*Z*+*E*)-acetaldehyde oxime (0.026 mL, 0.44 mmol, 2 equiv), Pd(OAc)₂ (4.9 mg, 0.022 mmol, 0.1 equiv) and triphenylphosphine (0.011 g, 0.044 mmol, 0.2 equiv) in EtOH:Water in an 1 mL flask (3:1 0.4 mL) were heated to reflux for 3

²⁶ BASF Patent US2003/153568 A1, 2003.

²⁷ Kim E.S., Kim H.S., Kim J.N., *Tetrahedron Lett.* **2009**, 50(17), 2973-2975

h under nitrogen atmosphere. The reaction mixture was filtered through a Celite pad and washed with EtOH/DCM (5 mL). After removal of solvent and column chromatographic purification process (Pentane:EtOAc 1:1) (R)-6-fluoro-2-(2-methylallyl)-1-oxo-2,3-dihydro-1*H*-indene-2-carboxamide (**13**) (0.045 g, 0.18 mmol, 83% yield) was obtained as a yellow oil.

Rf: 0.15 (Pentane:Ethyl Acetate 1:1).

¹H NMR (400 MHz, Chloroform-*d*) δ 7.45 (m, 1H, Ar*H*), 7.42 – 7.30 (m, 2H, Ar*H*), 6.98 (s, 1H, *NH*₂), 5.57 (s, 1H, *NH*₂), 4.86 (s, 1H, CCH₂), 4.78 (s, 1H, CCH₂), 3.99 (d, *J* = 17.8 Hz, 1H, CH₂), 3.16 (d, *J* = 17.8 Hz, 1H, CH₂), 2.73 (d, *J* = 13.0 Hz, 1H, CH₂CMe), 2.63 (d, *J* = 13.0 Hz, 1H, CH₂CMe), 1.63 (s, 3H, CH₃).

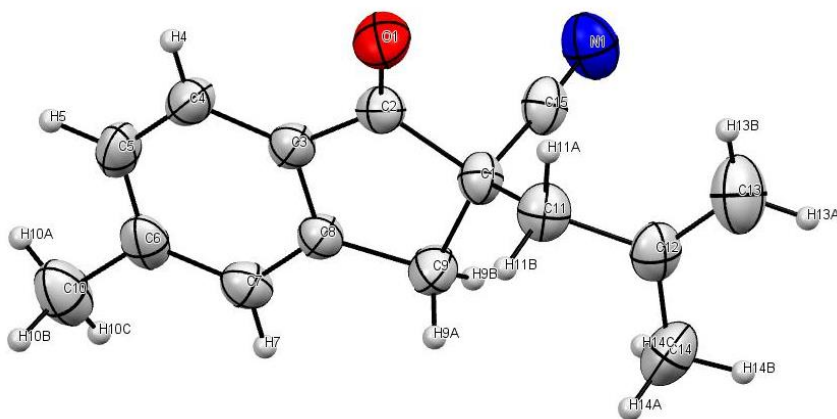
¹³C NMR (101.00 MHz, Chloroform-*d*) δ 205.7, 171.5, 162.4 (d, *J* = 248.8 Hz), 149.5 (d, *J* = 2.0 Hz), 140.6, 136.3 (d, *J* = 7.3 Hz), 128.1 (d, *J* = 7.9 Hz), 123.8 (d, *J* = 23.8 Hz), 116.9, 110.19 (d, *J* = 22.0 Hz), 61.8, 46.9, 33.7, 23.2.

IR ν_{max} 3726 (w), 3629 (w), 3599 (w), 3449 (w), 3347 (w), 2271 (w), 1705 (s), 1685 (s), 1610 (w), 1489 (m), 1444 (w), 1371 (w), 1267 (m), 904 (w), 881 (w).

HRMS (ESI) calcd for C₁₄H₁₄FNNaO₂⁺ [*M*+Na]⁺ 270.0901; found 270.0903.

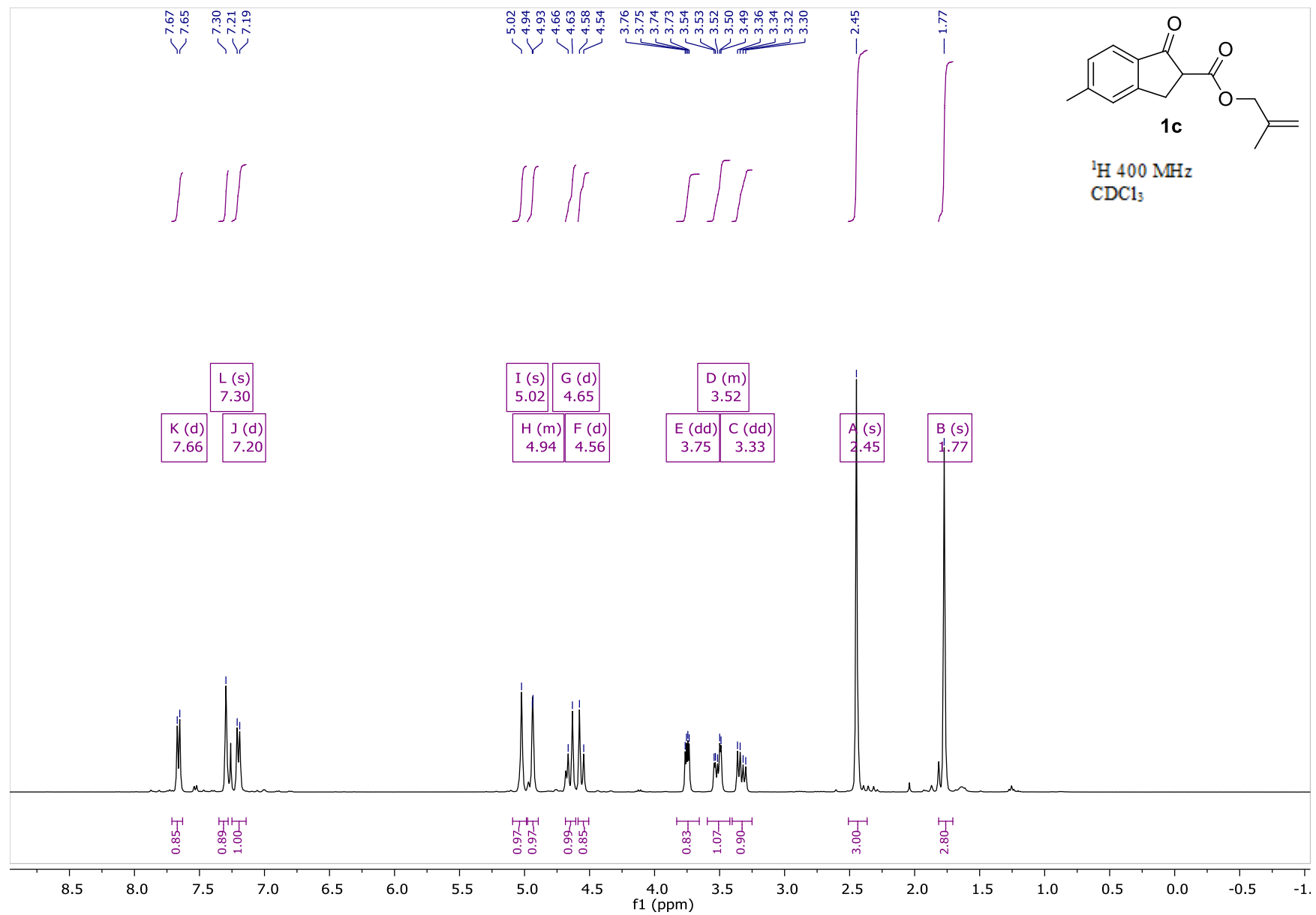
[α]_D^{25.0} +26.1 (c = 2.6, CHCl₃).

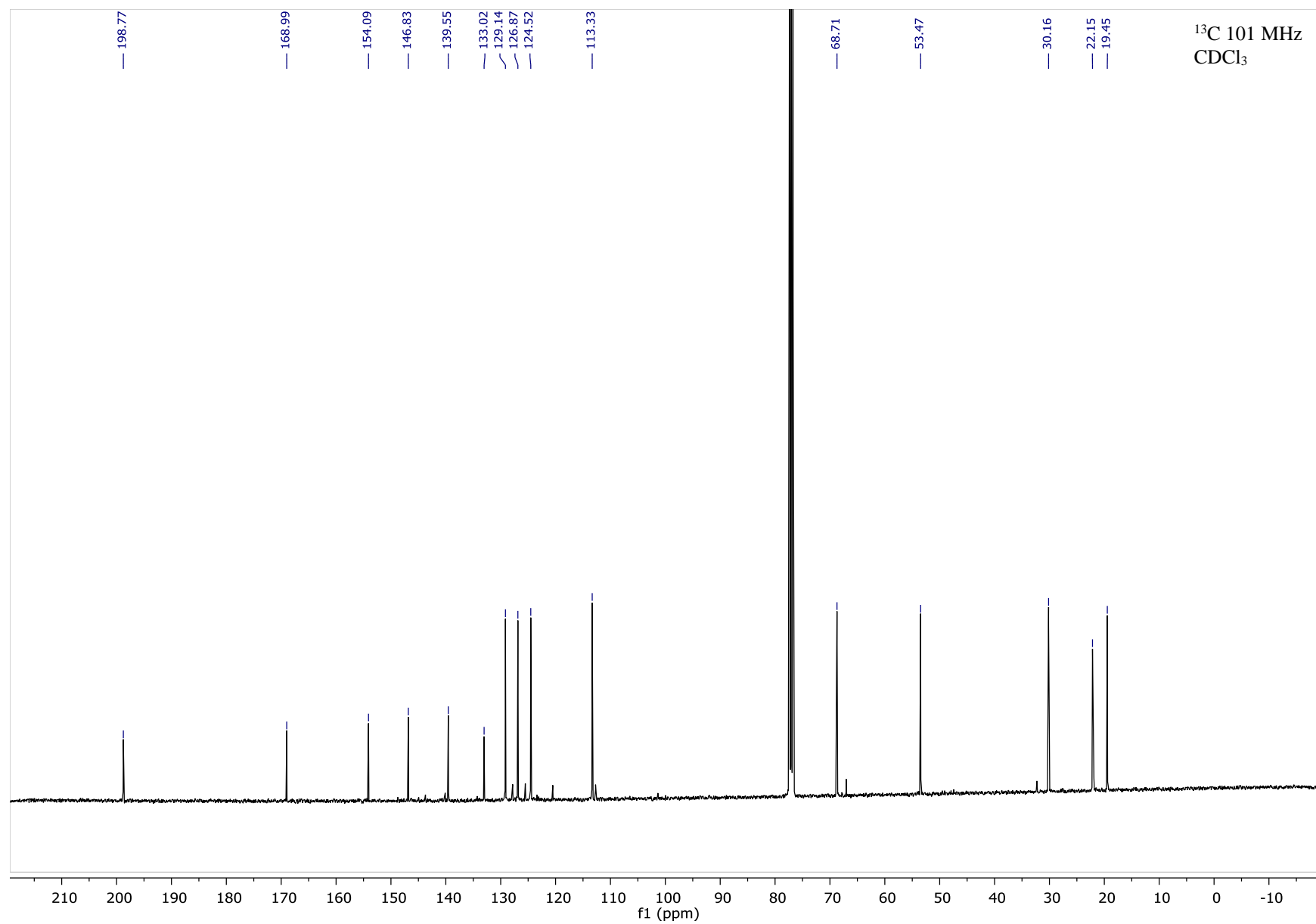
7. Result of the XRD experiment

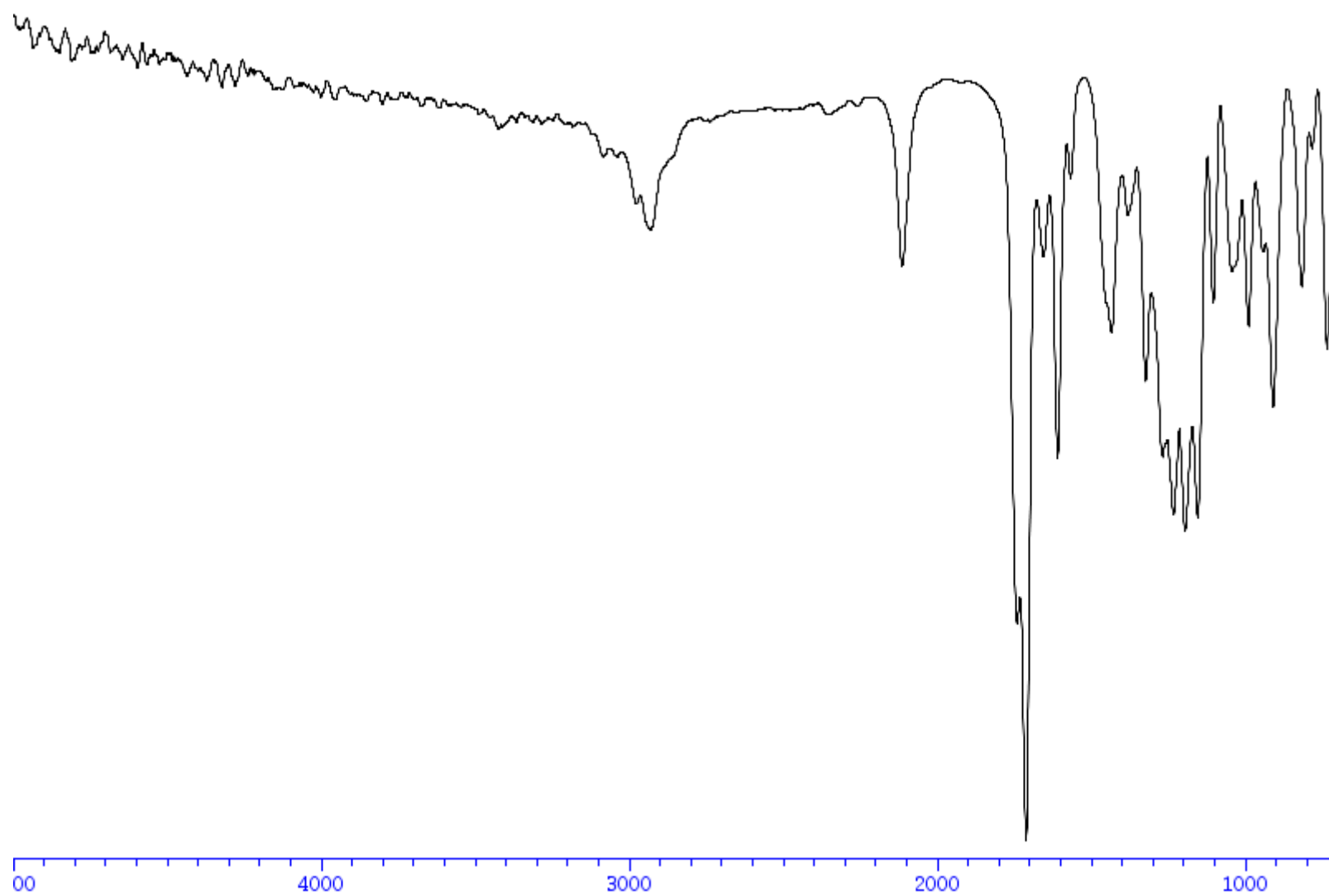


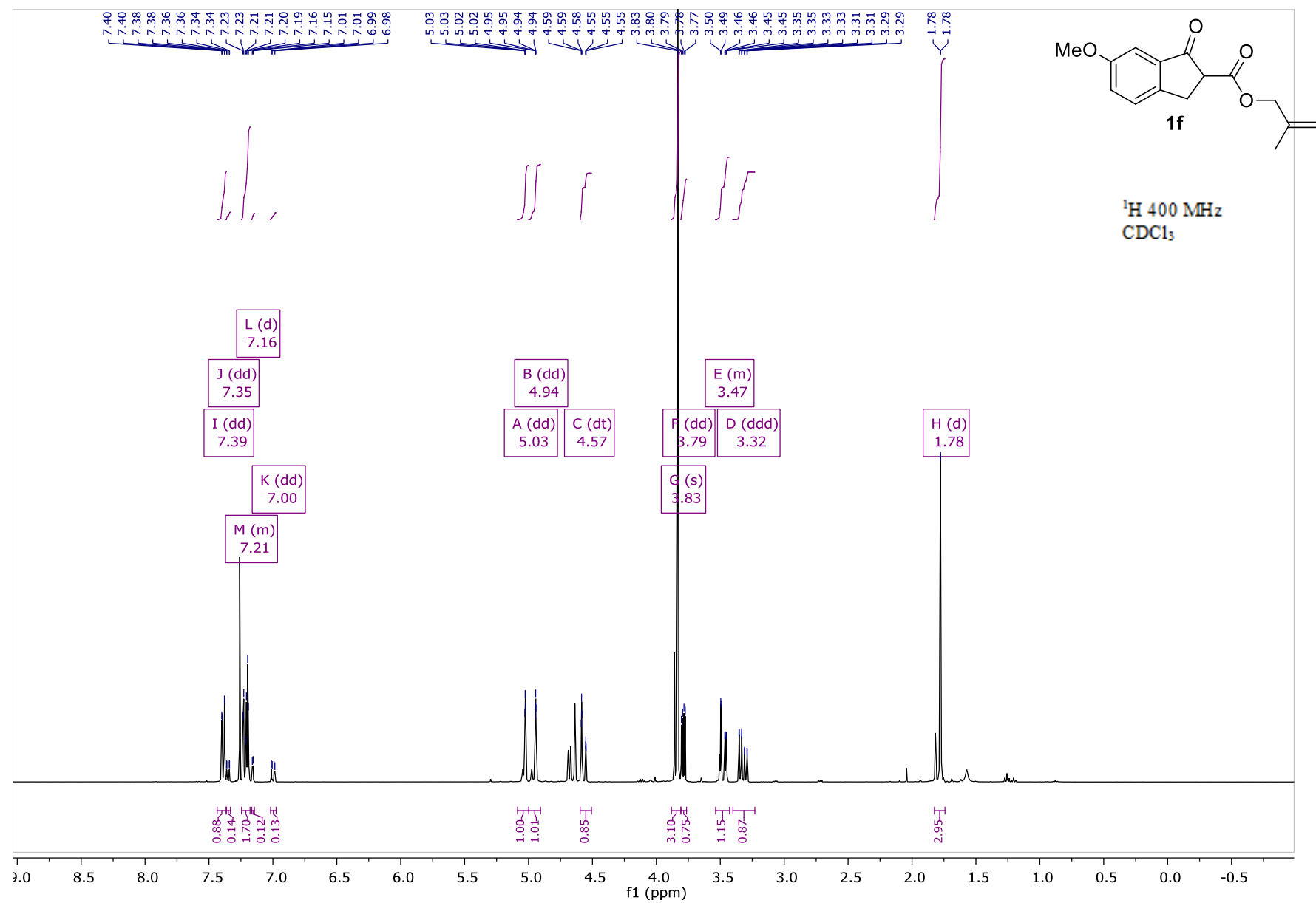
A single crystal was grown by slow diffusion of the solution of **8c** in EtOAc/heptane mixture. Supplementary crystallographic data for this compound have been deposited at Cambridge Crystallographic Data Centre (CCDC 1418044) and can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif.

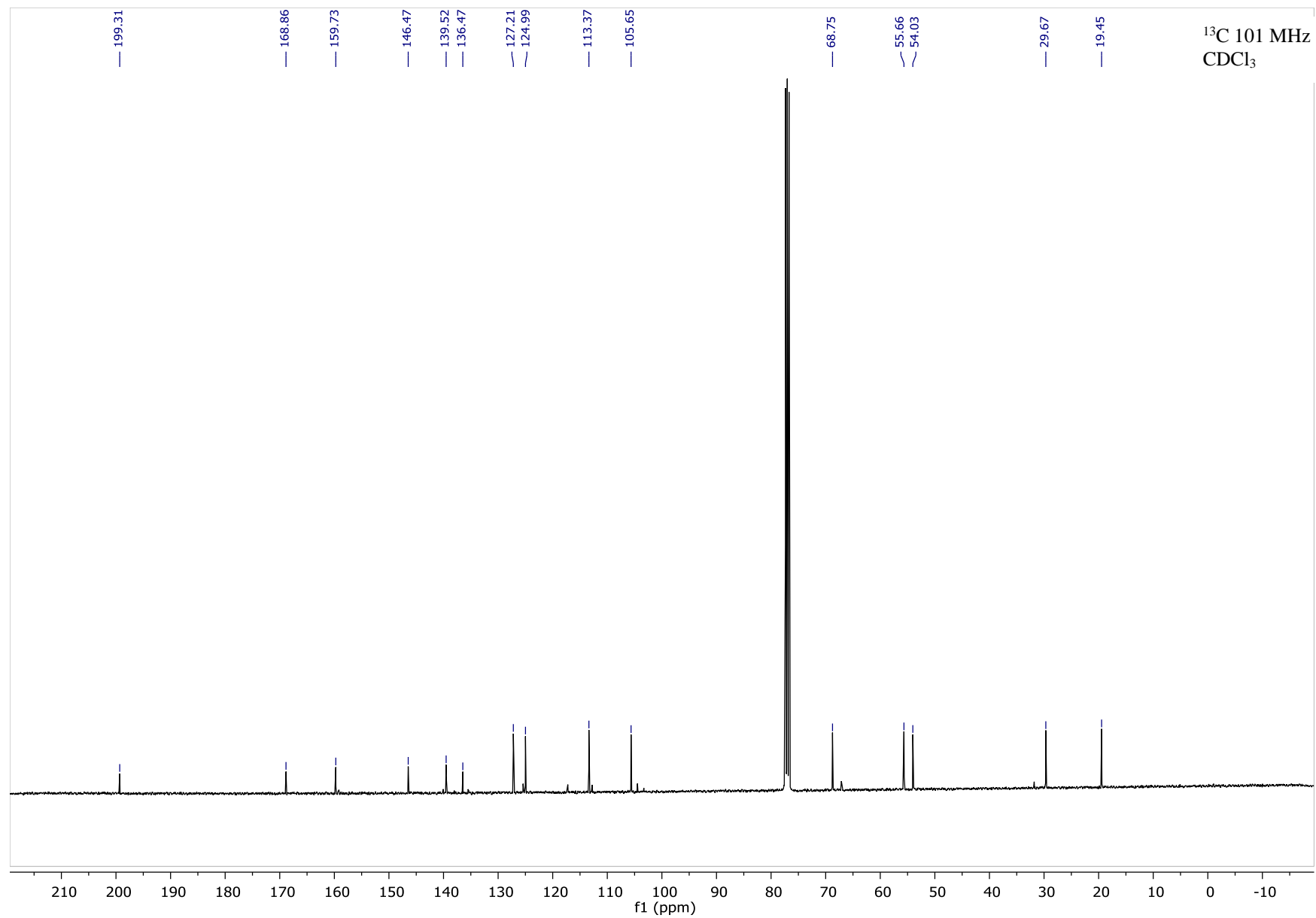
9. **Spectra of new compounds**

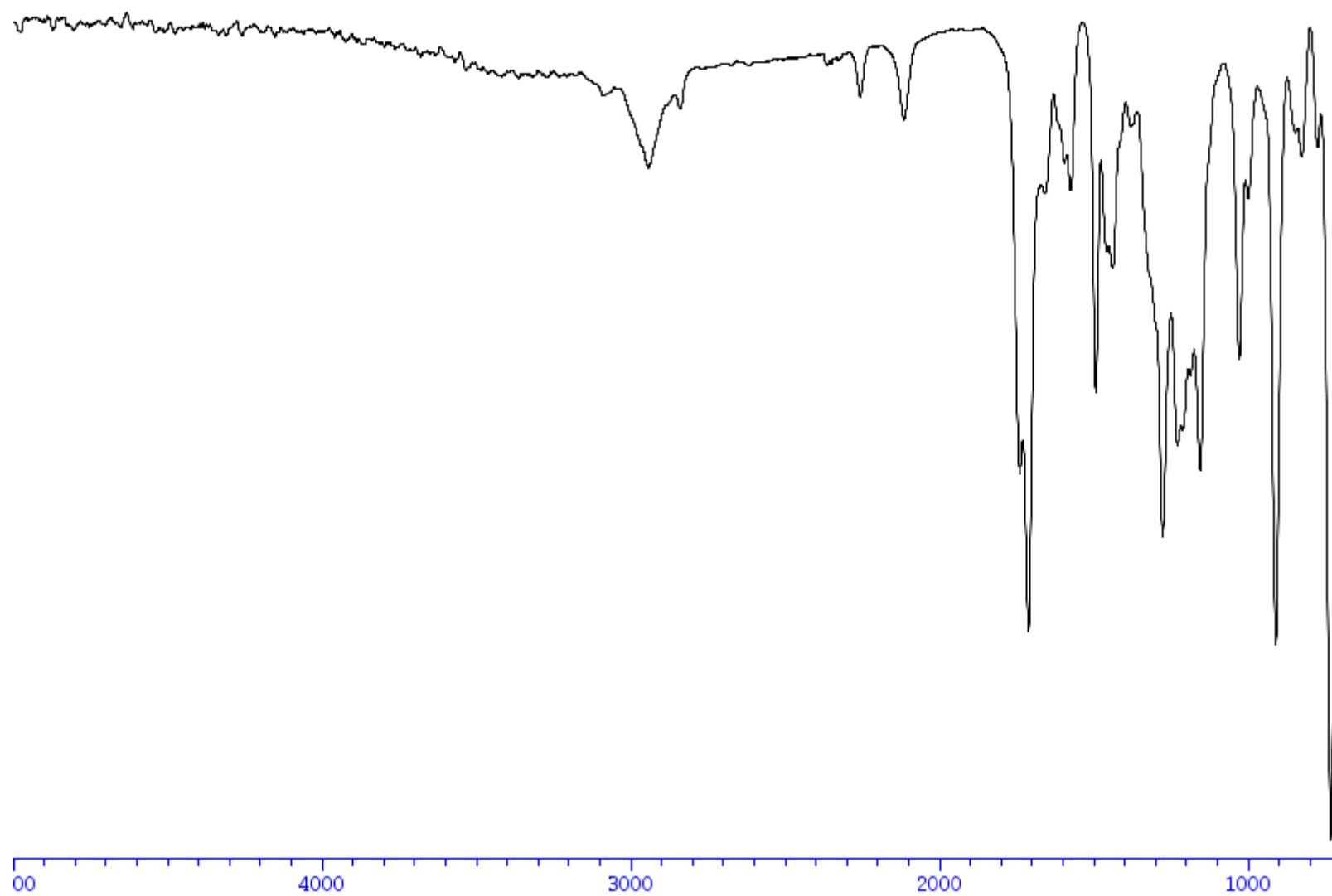


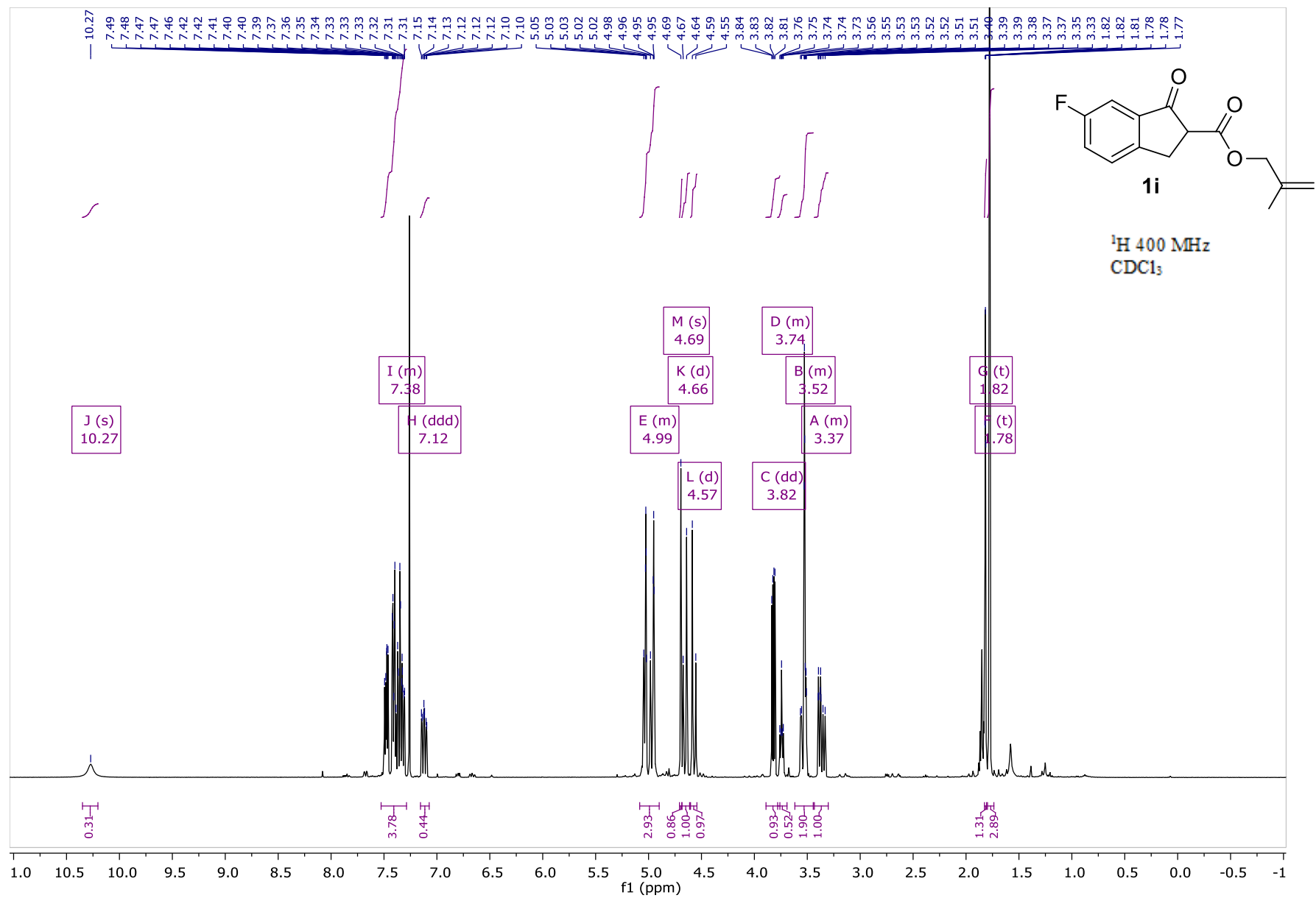


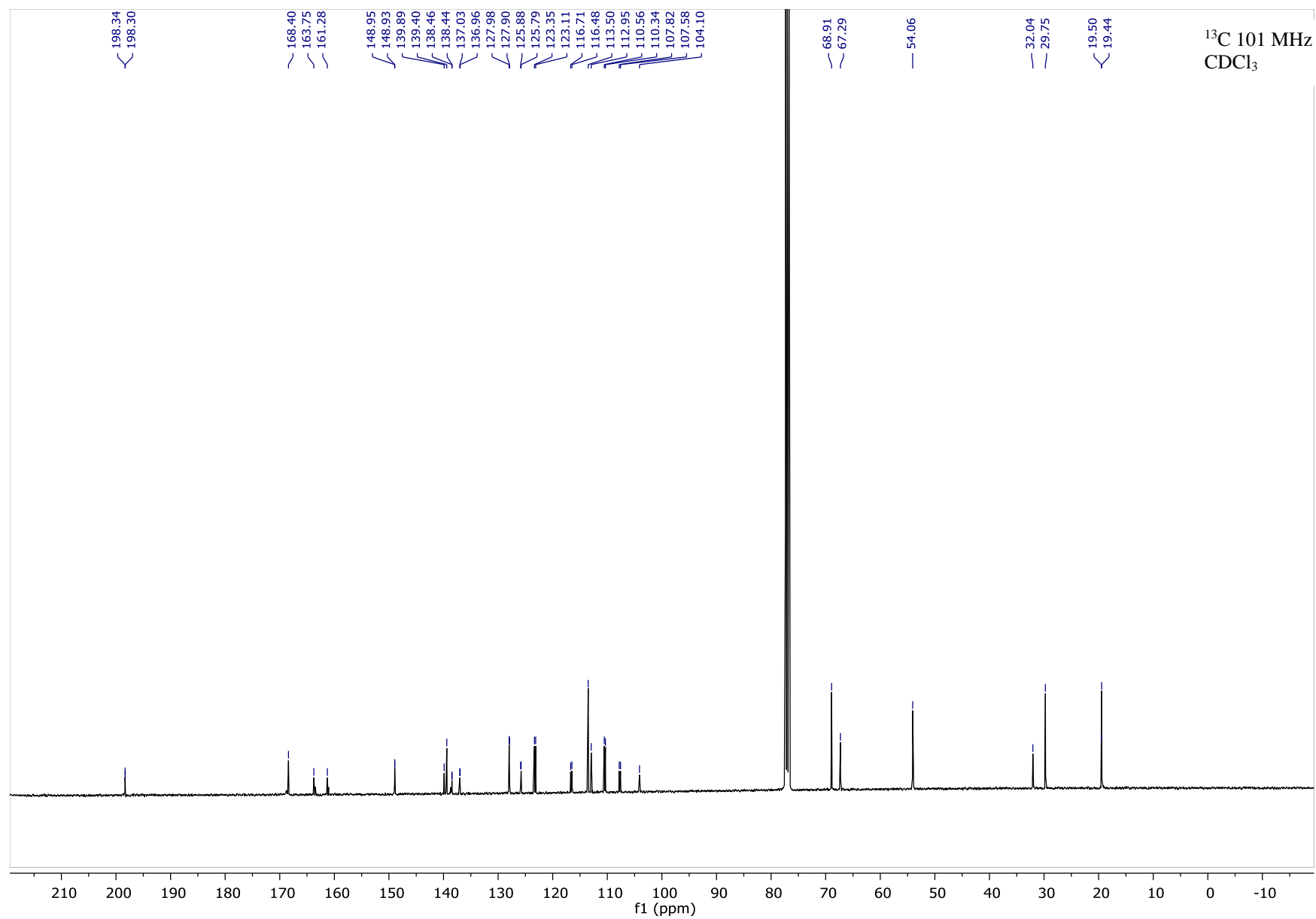


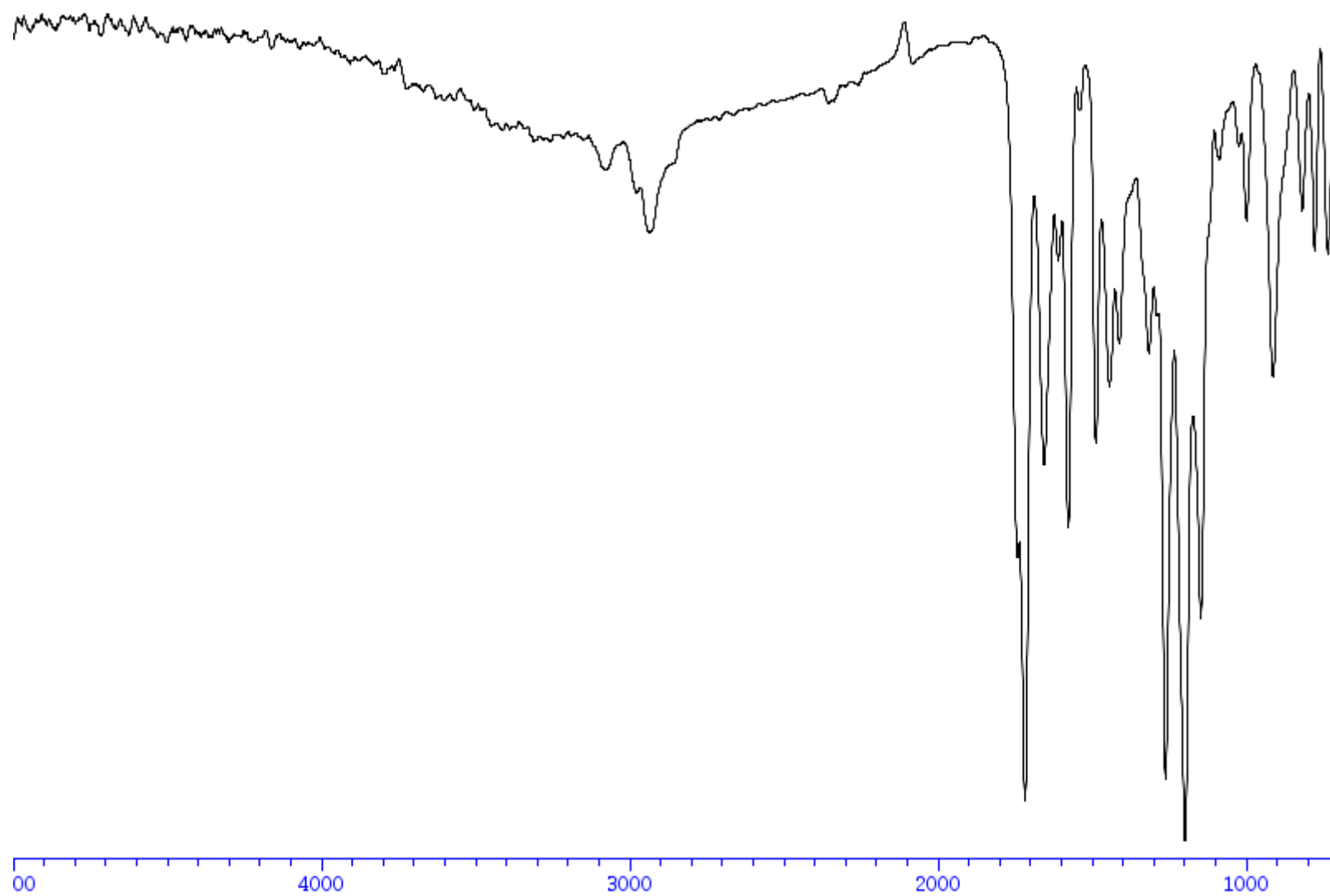


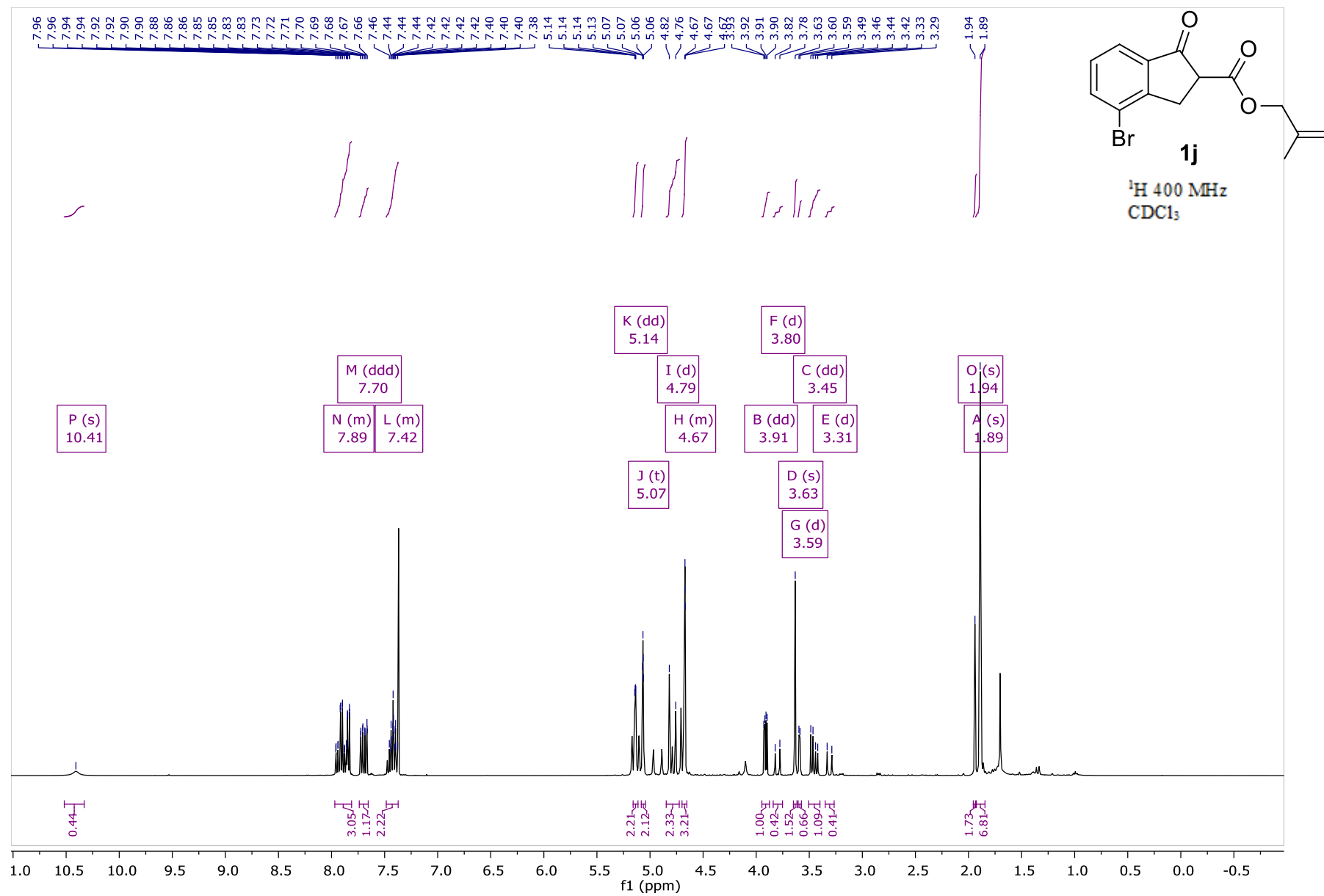


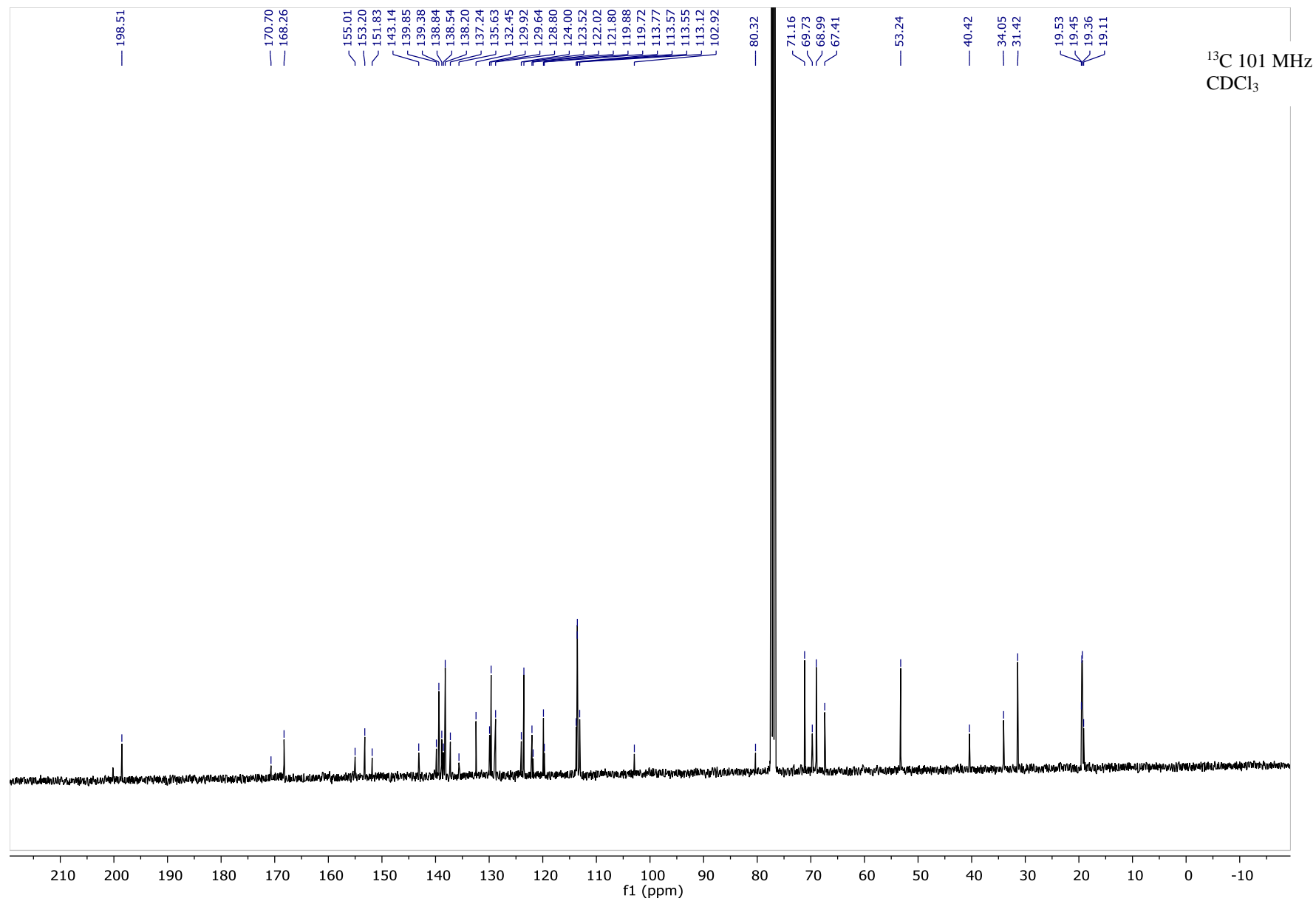


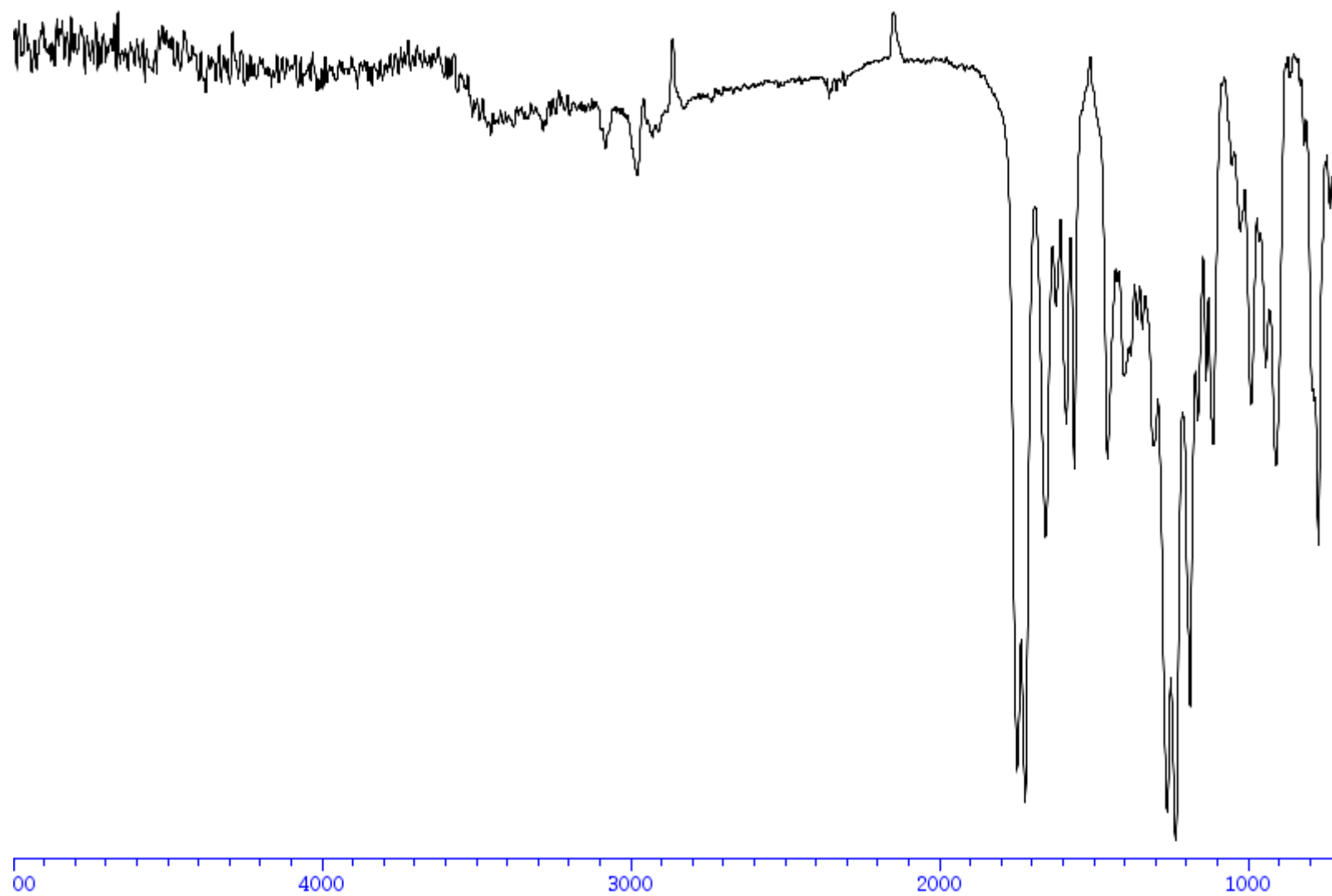


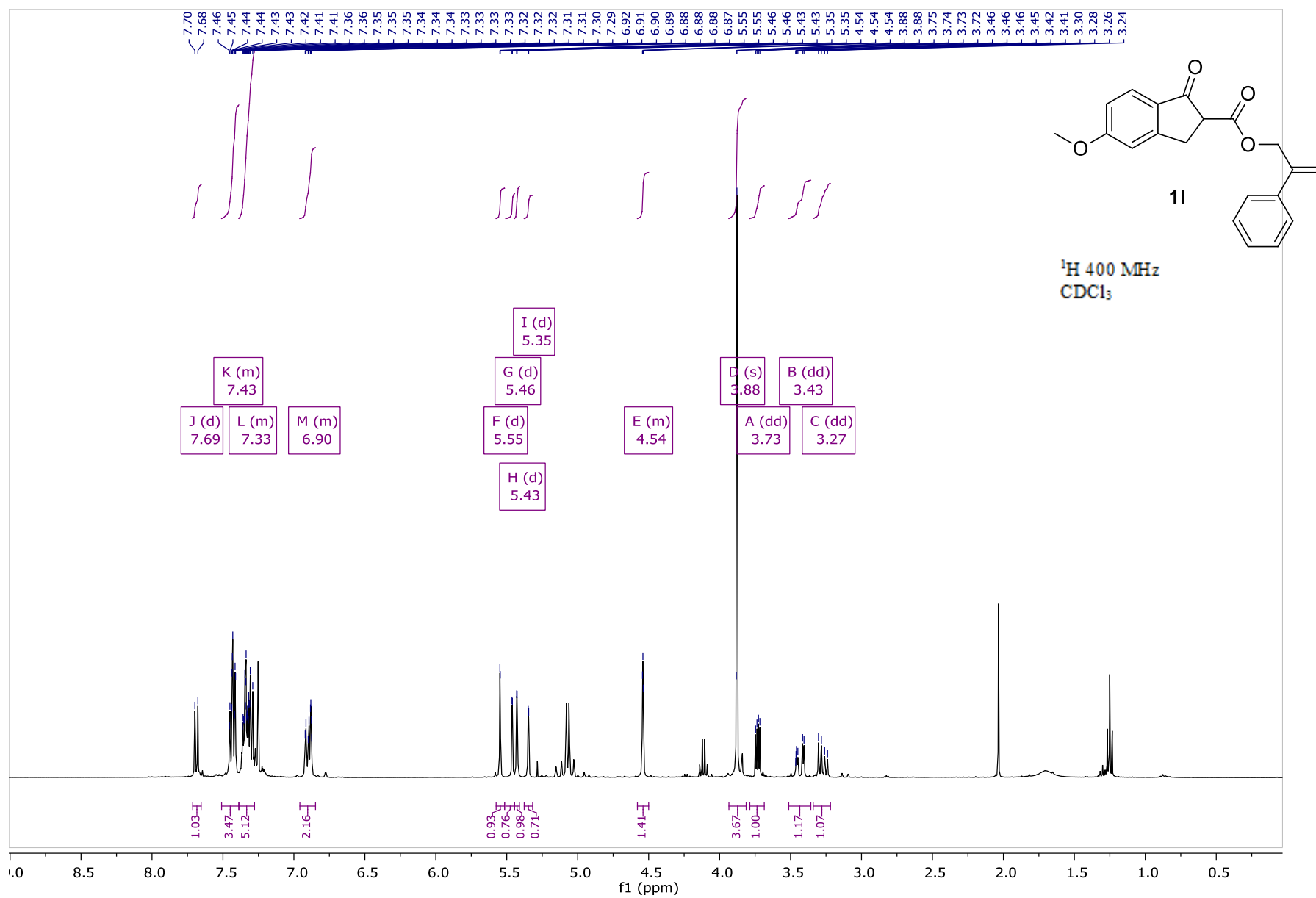


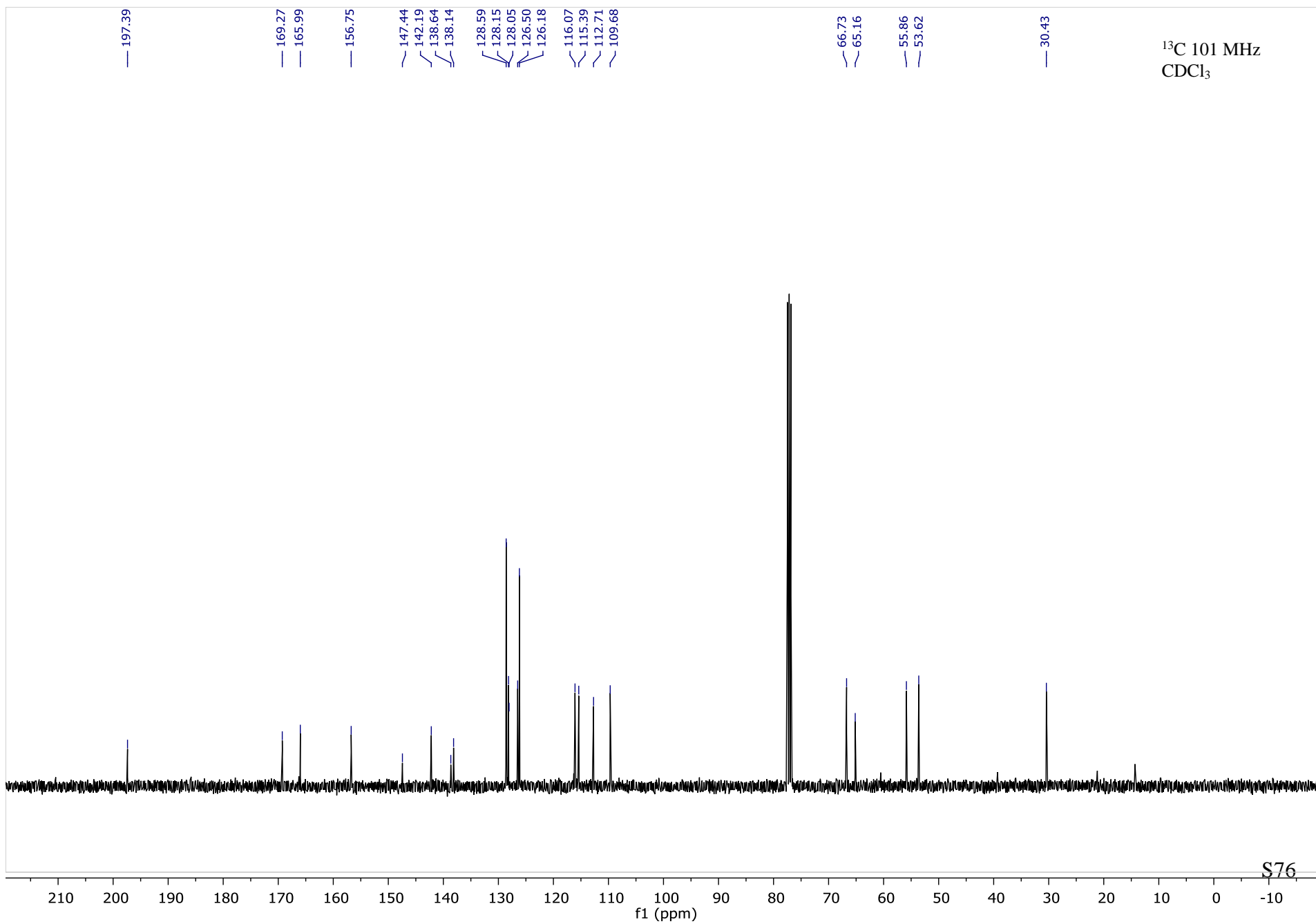


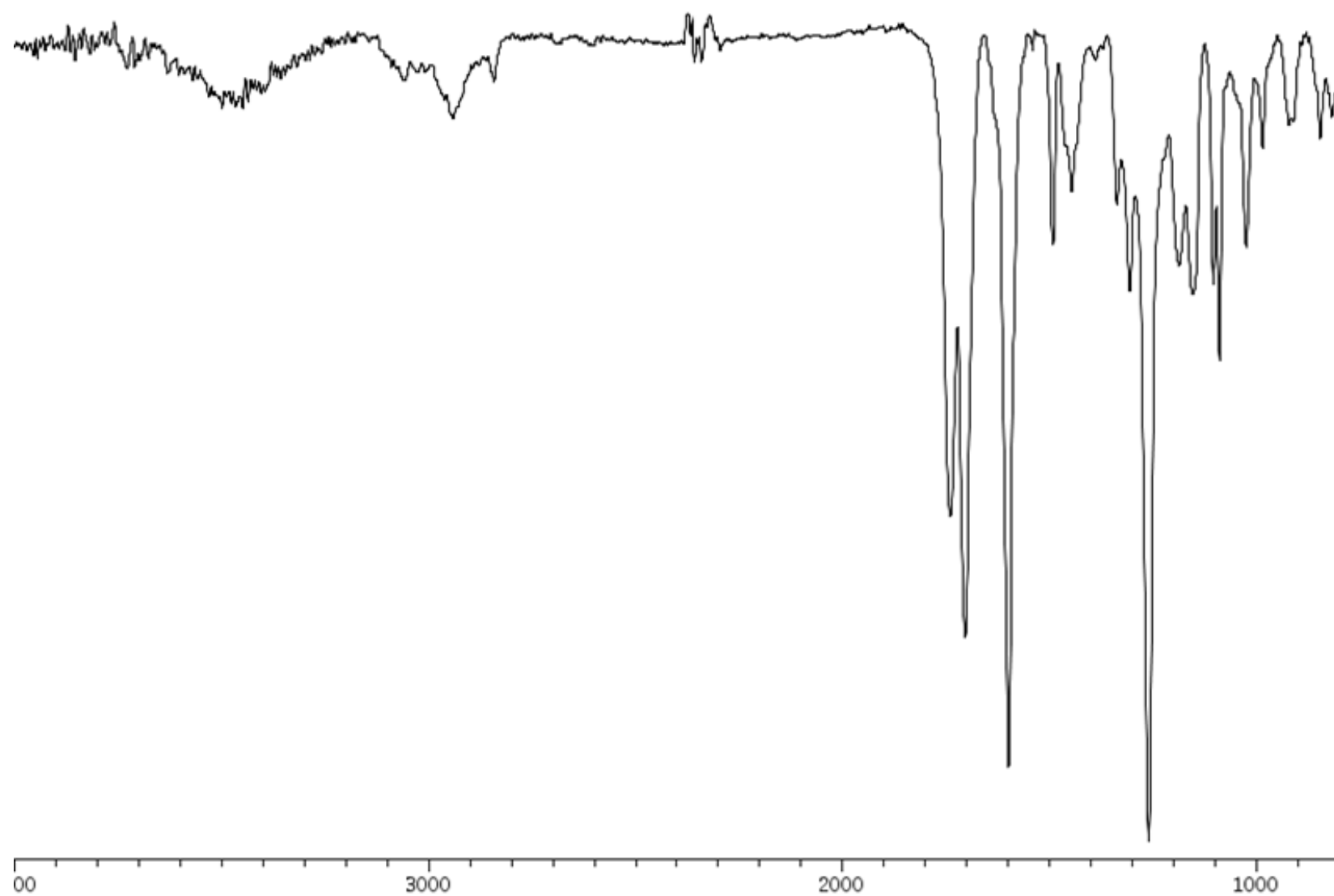


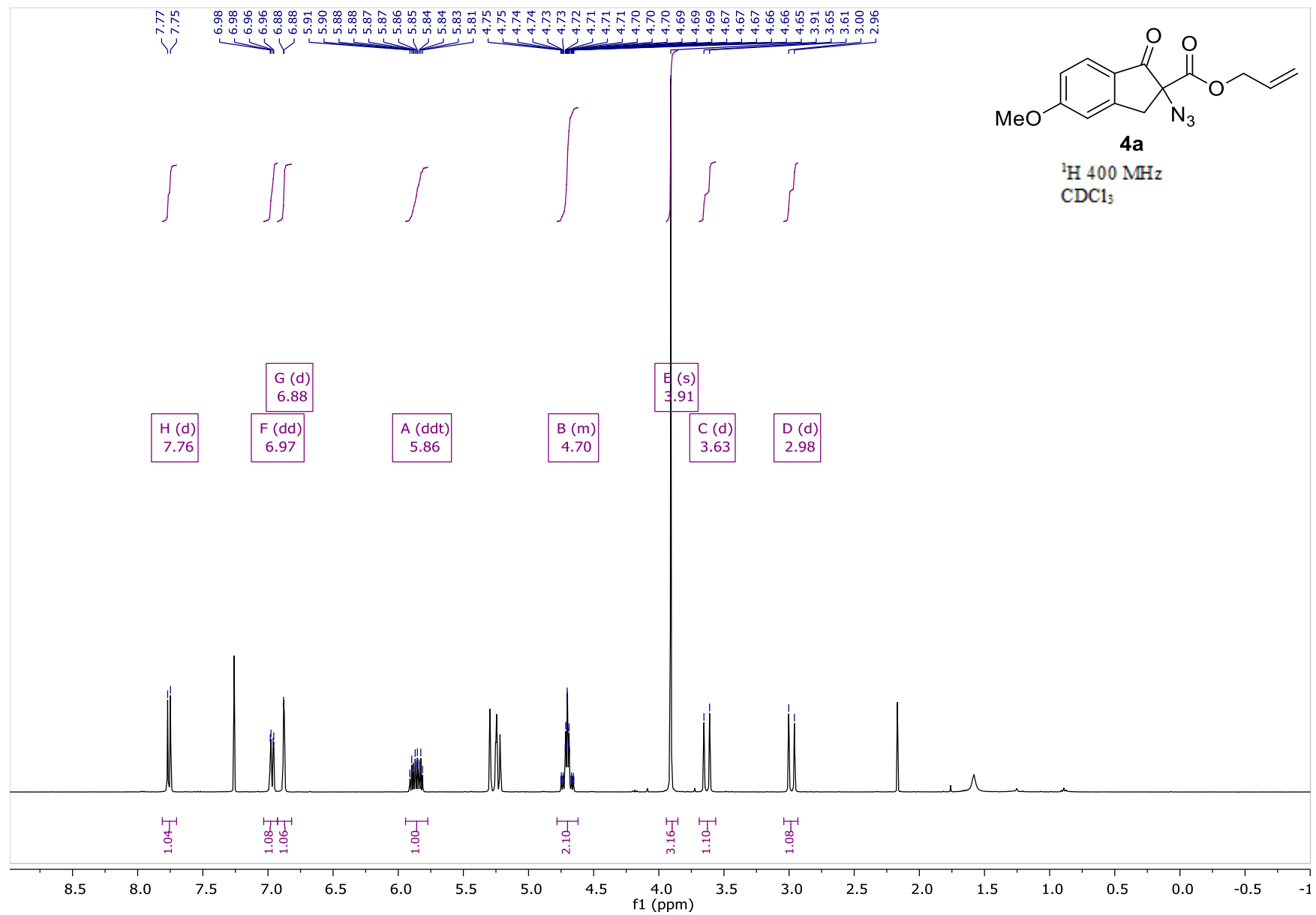


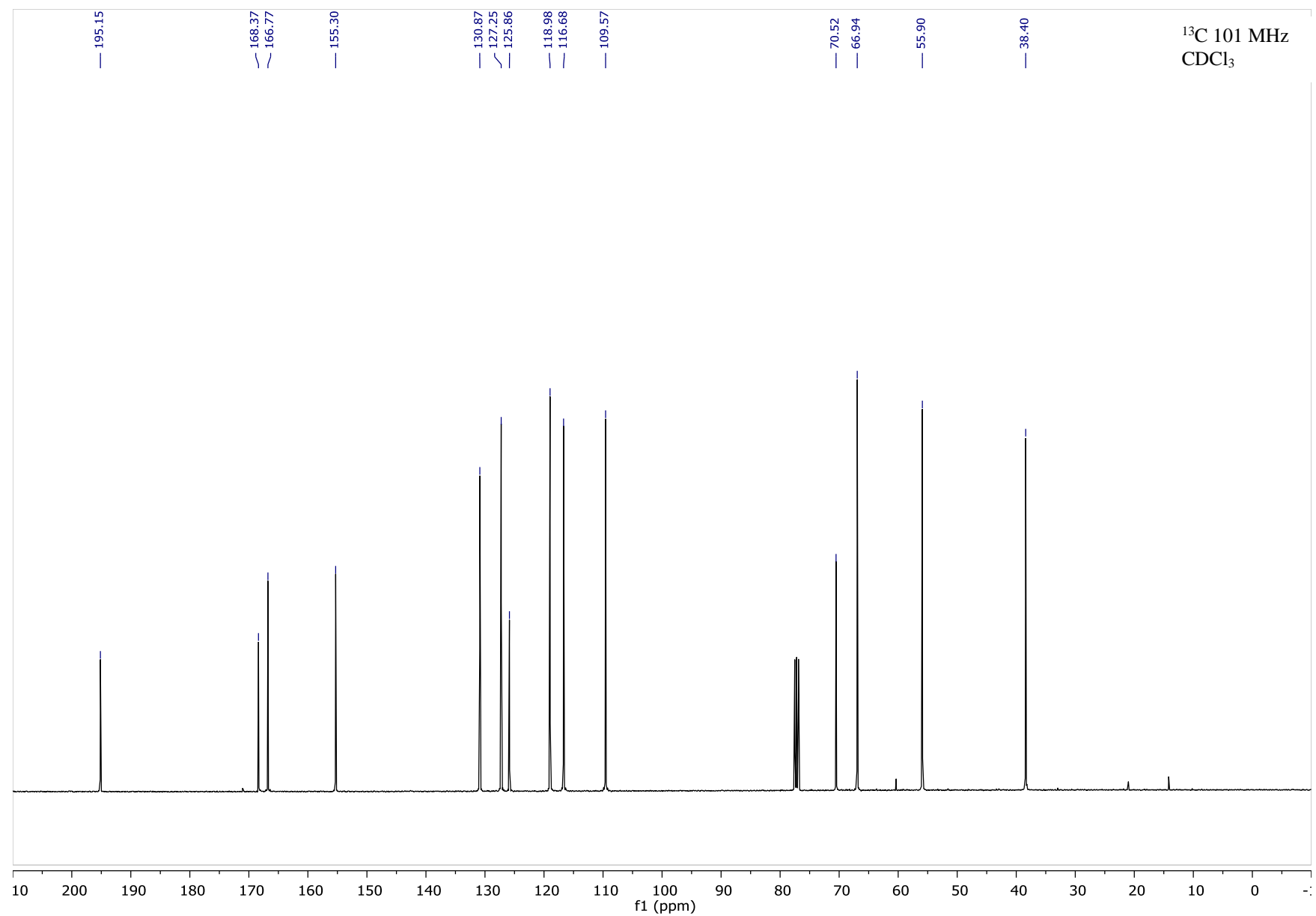


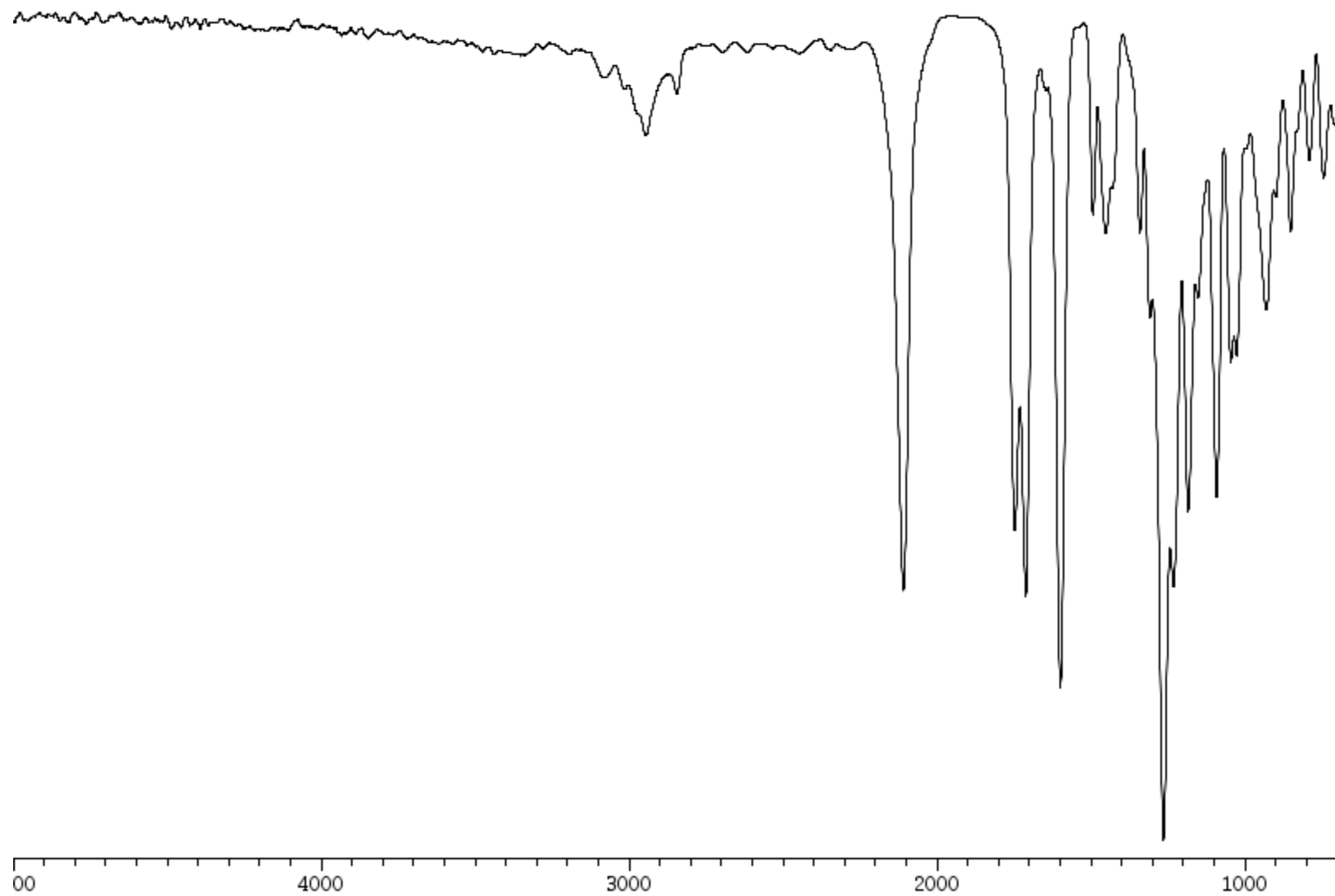


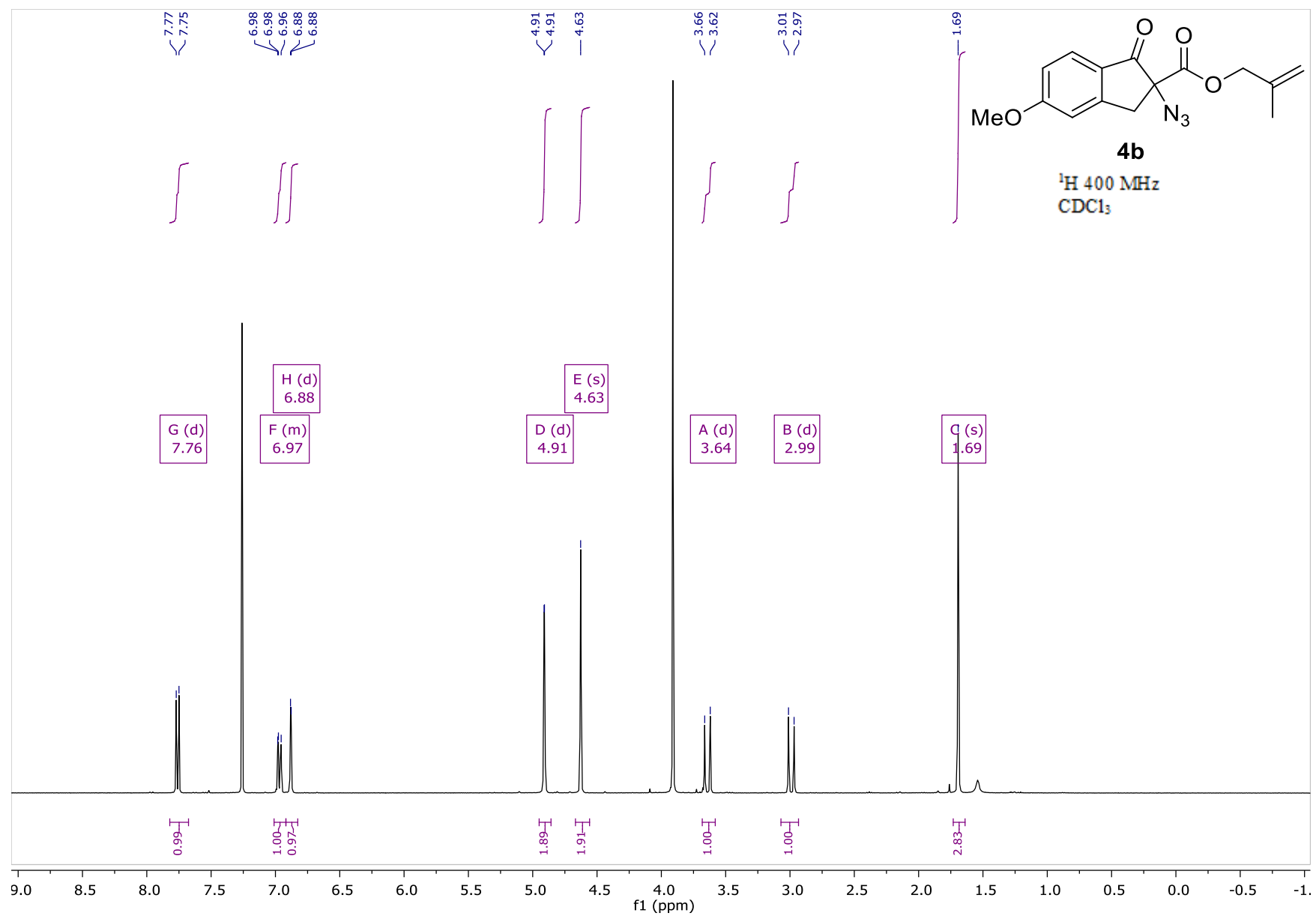


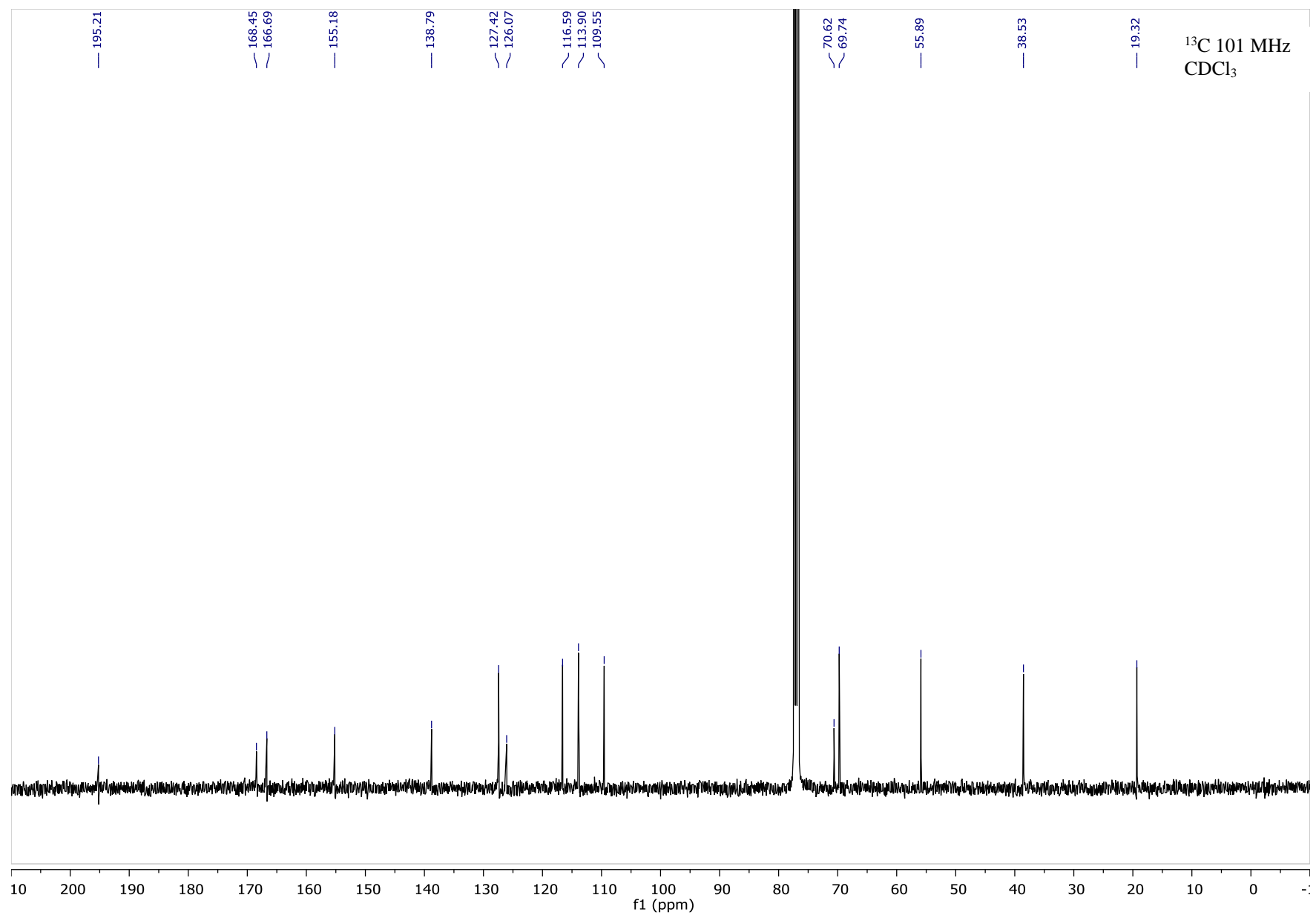


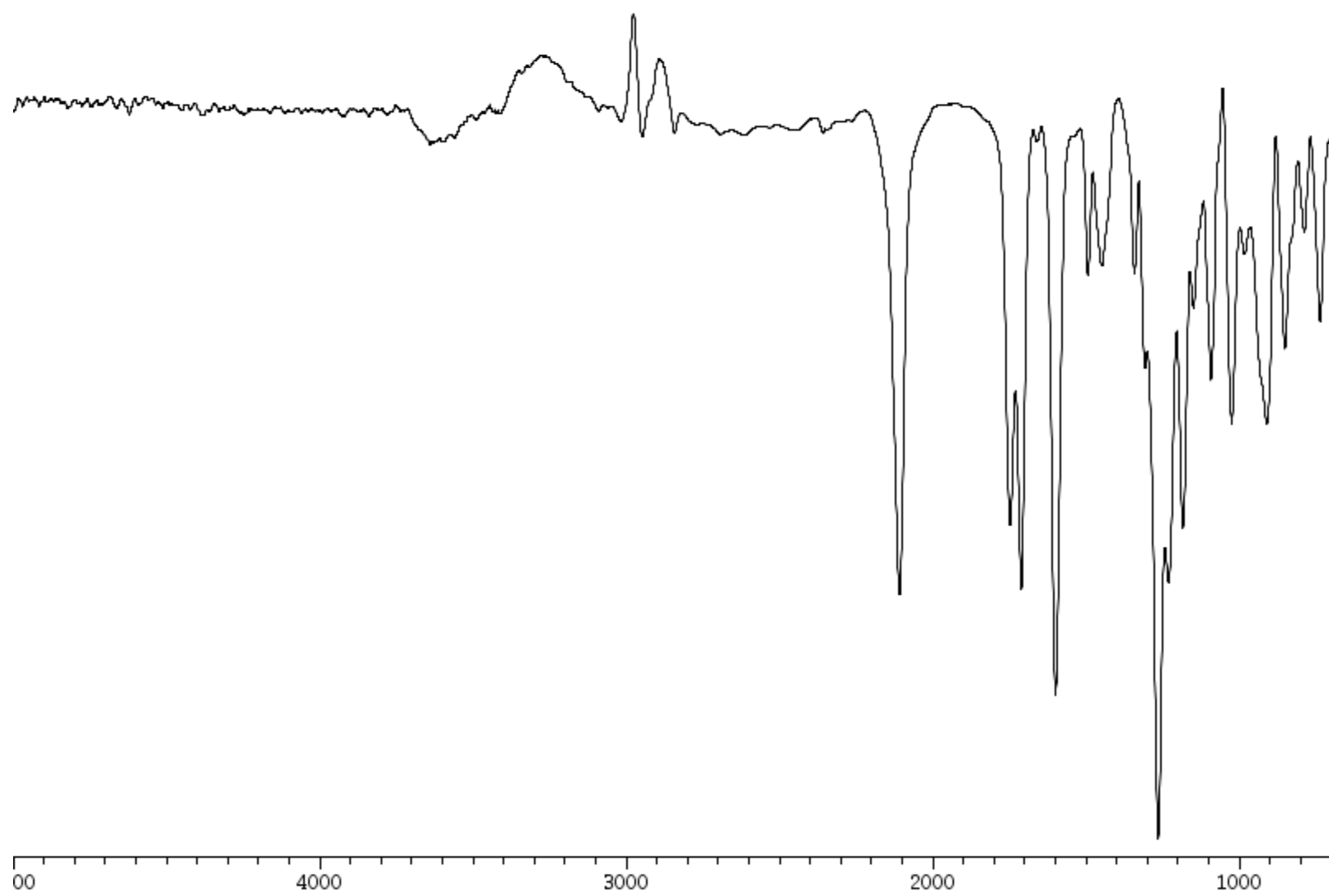


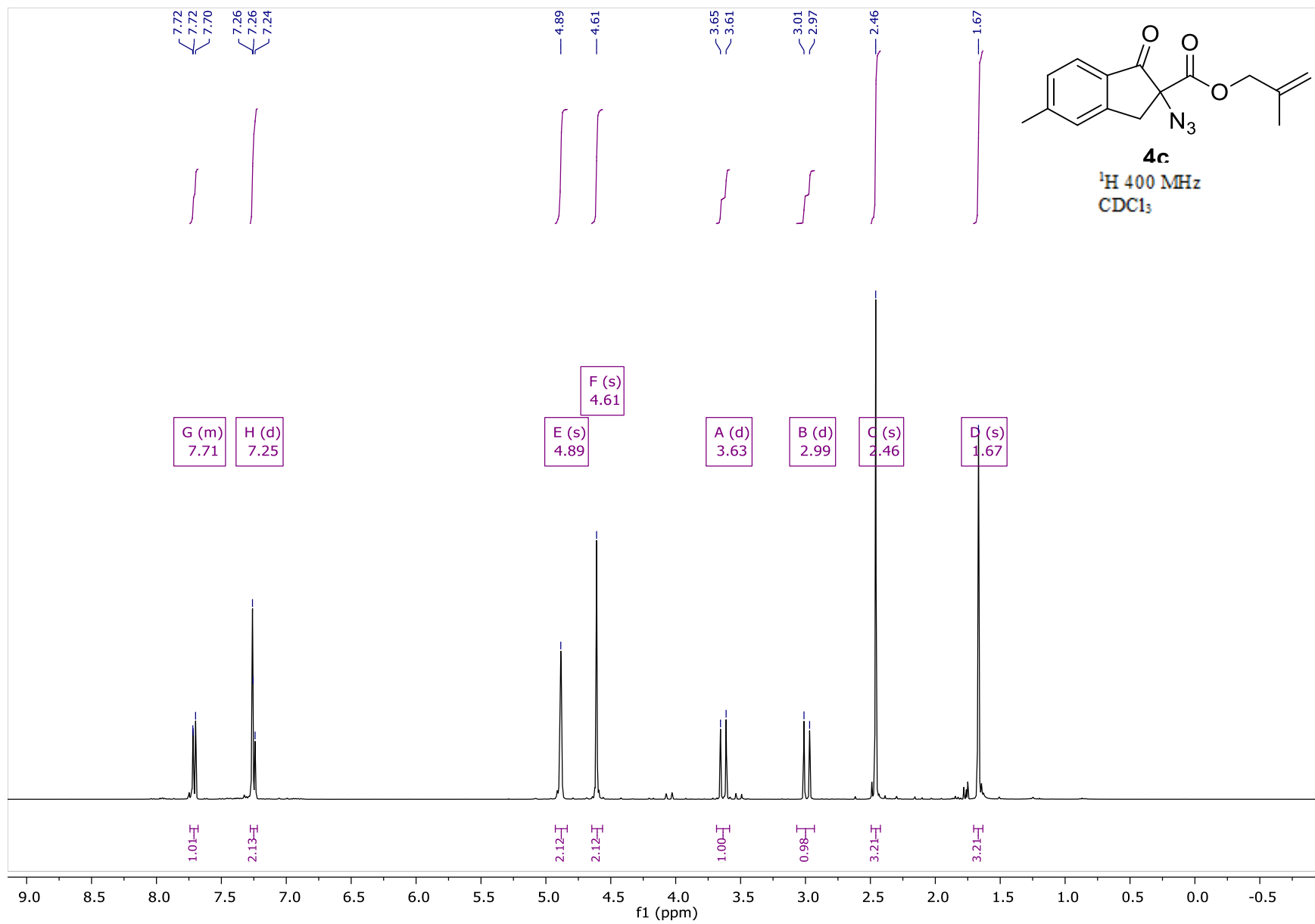


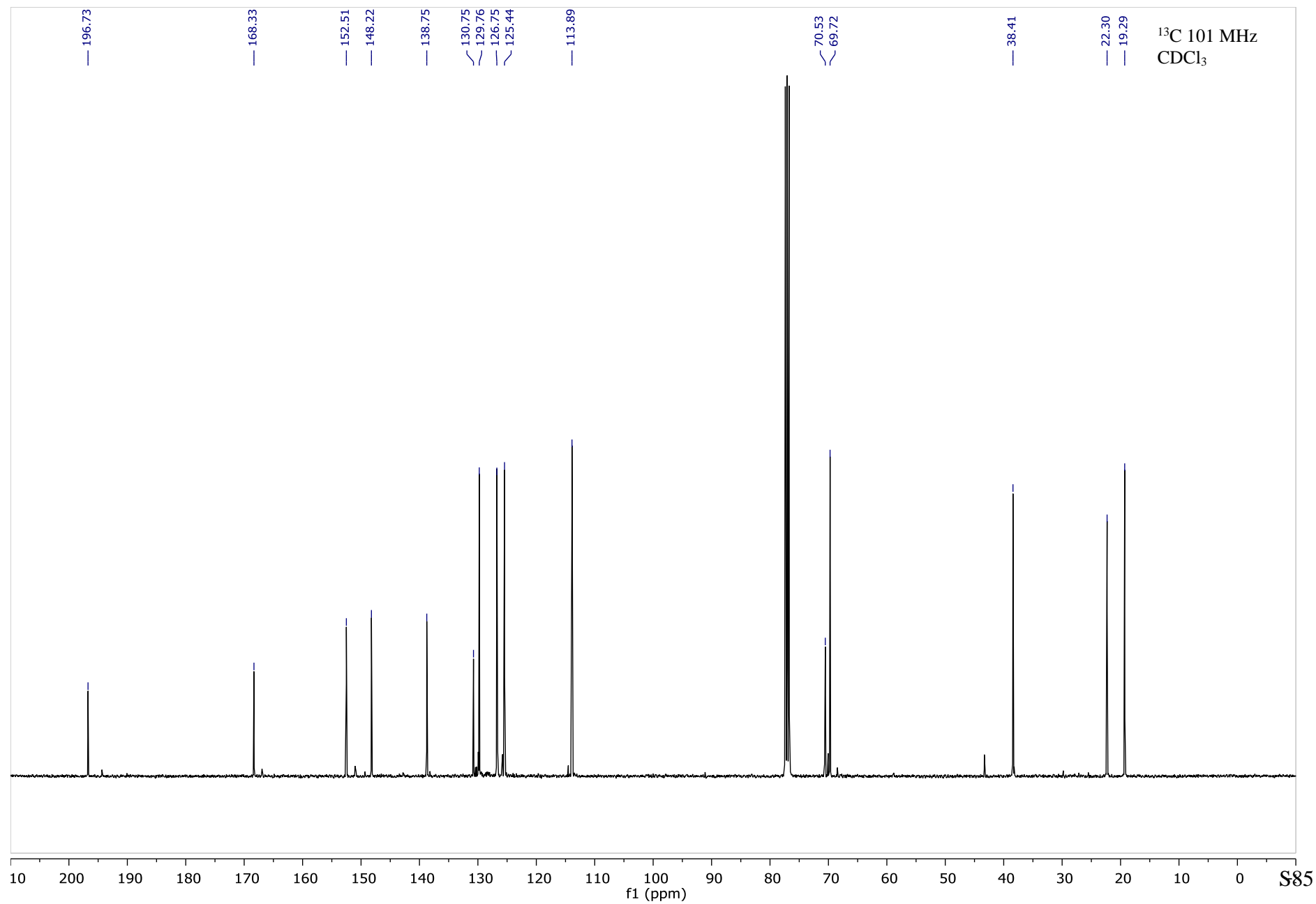


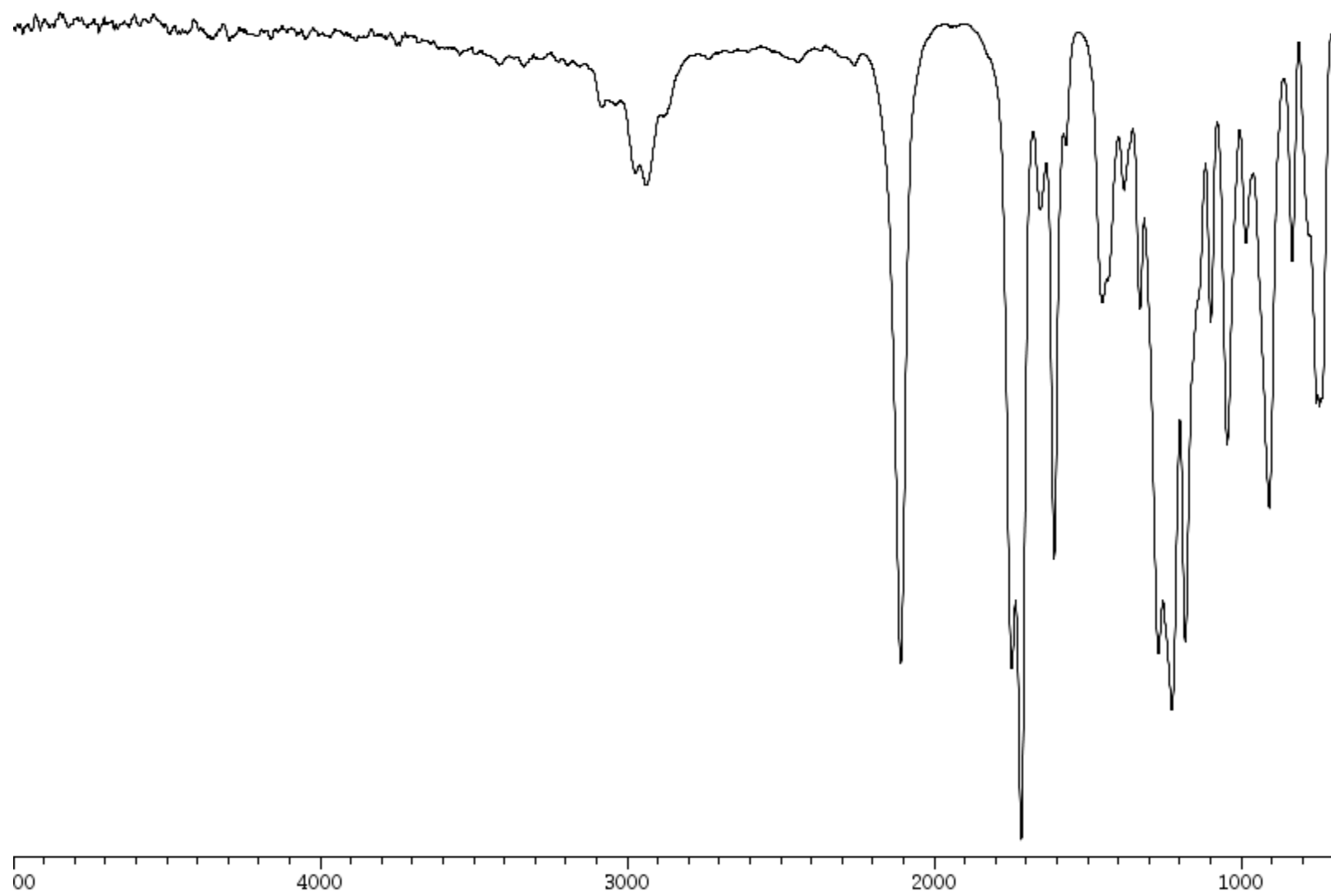


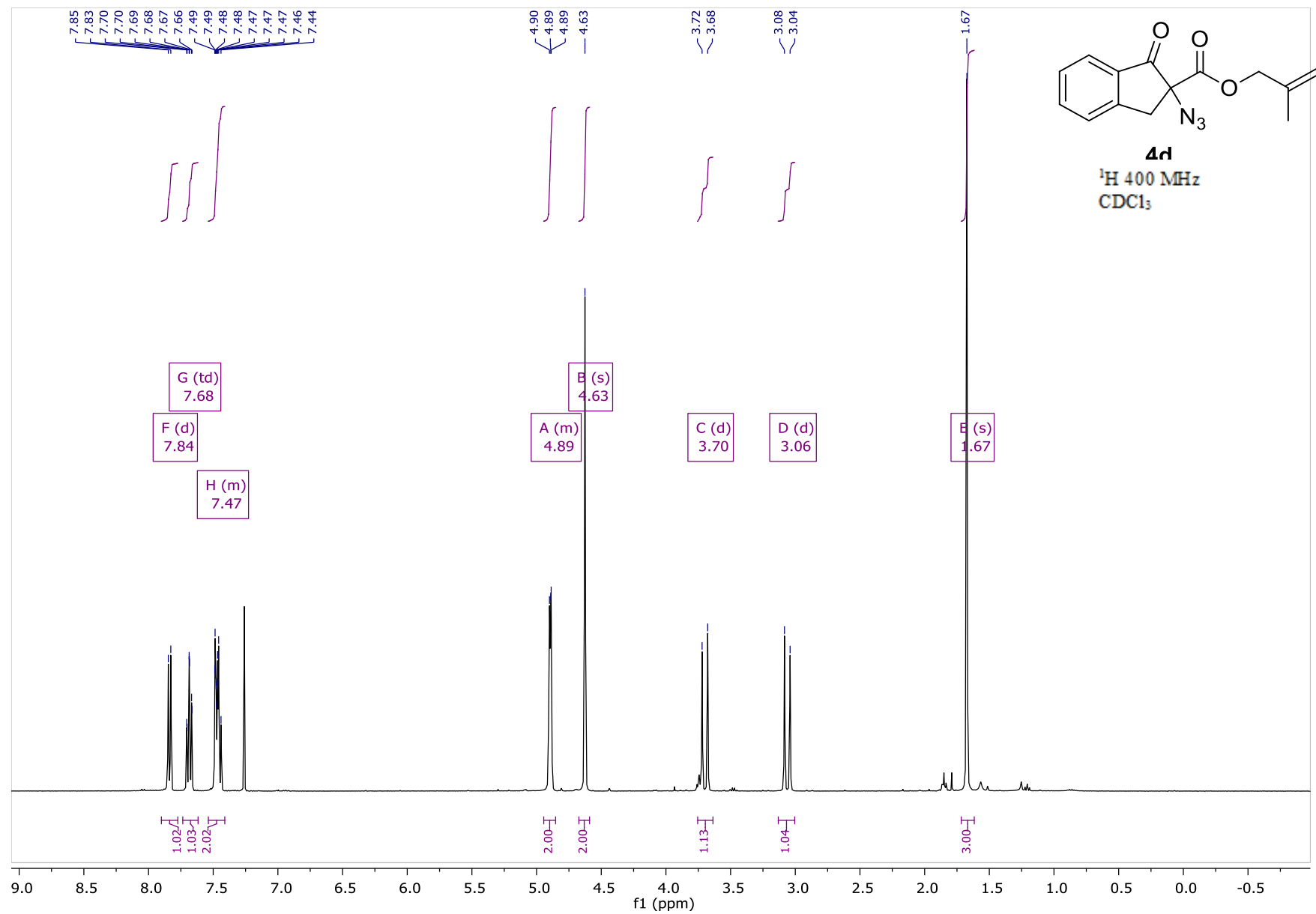


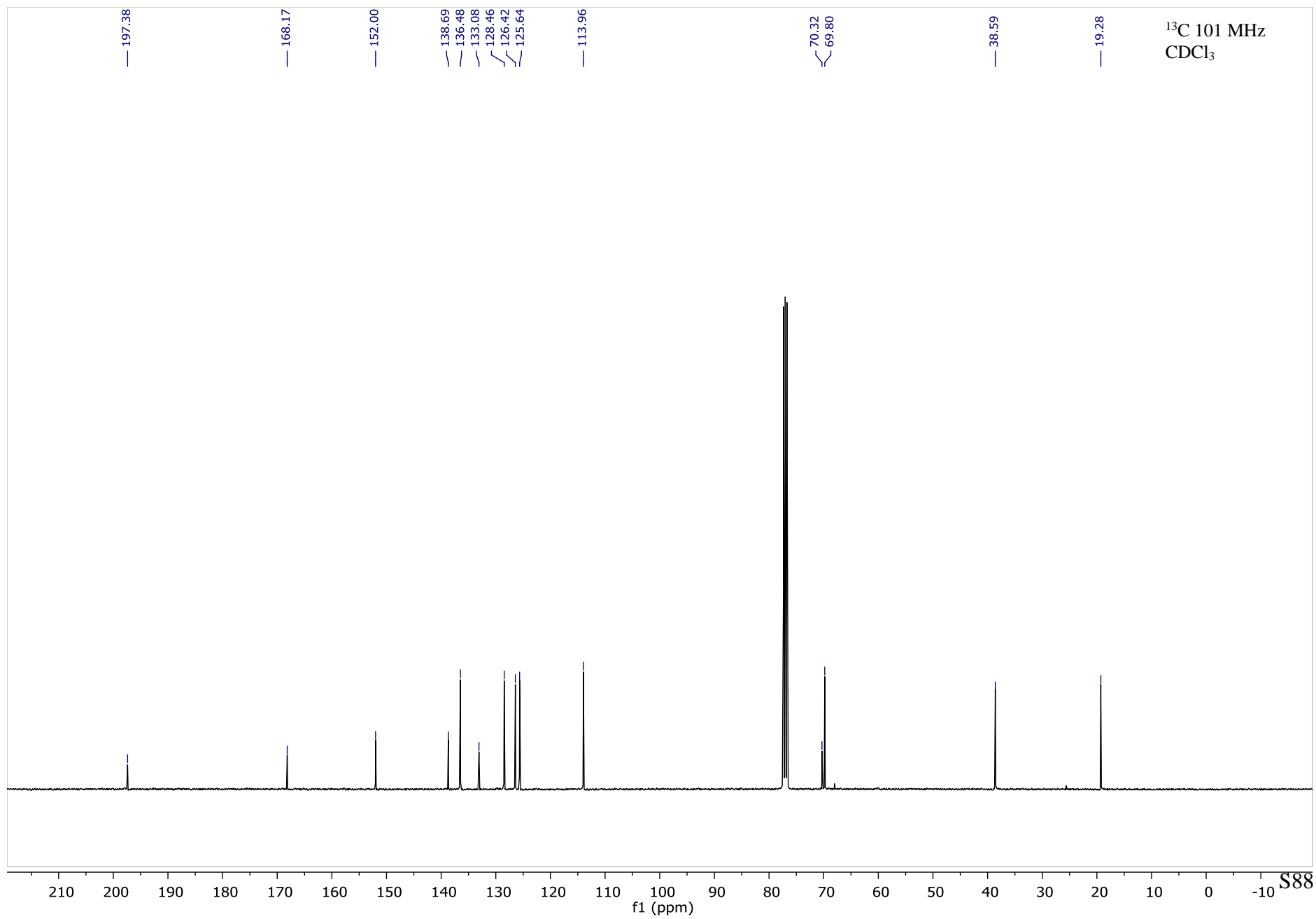


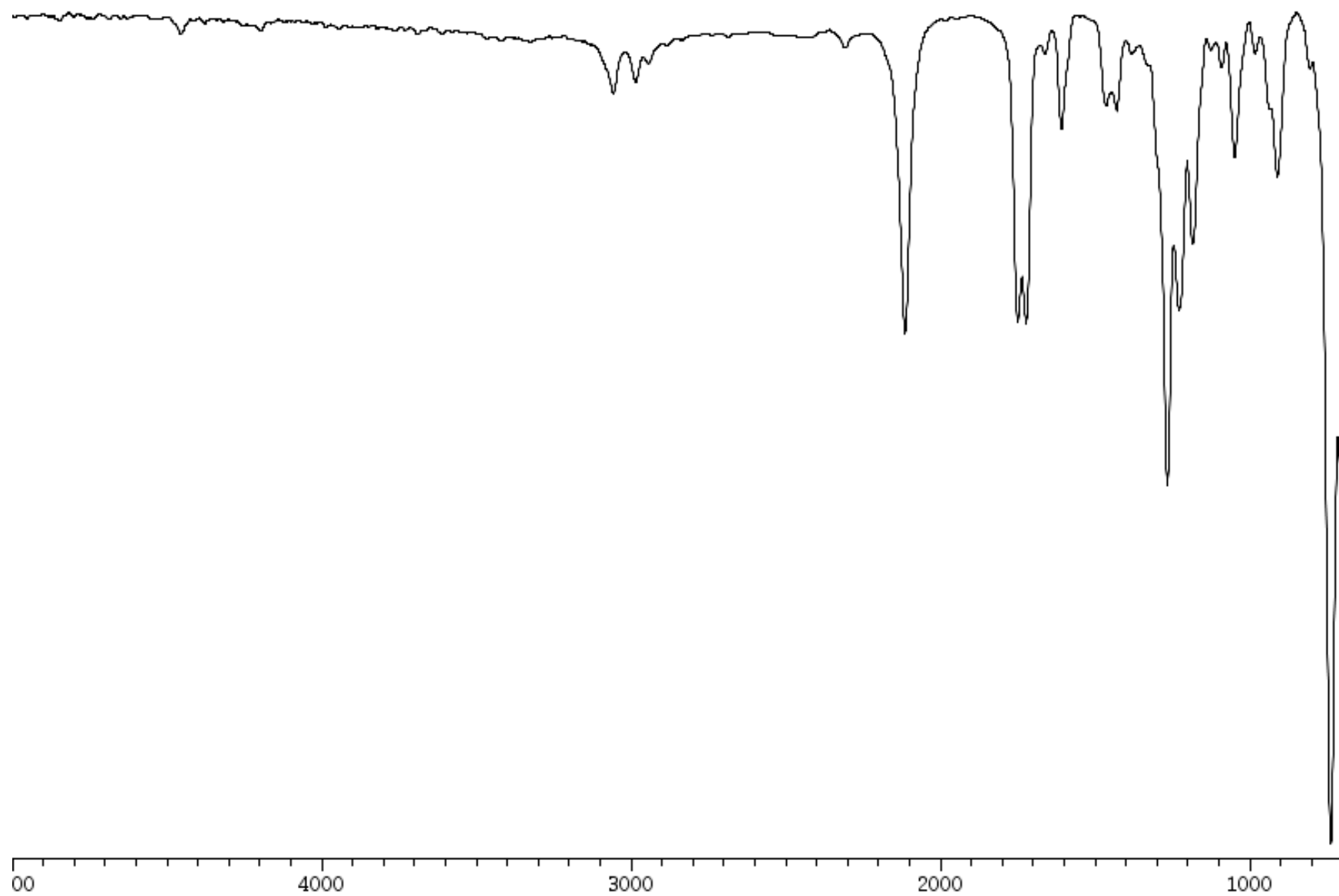


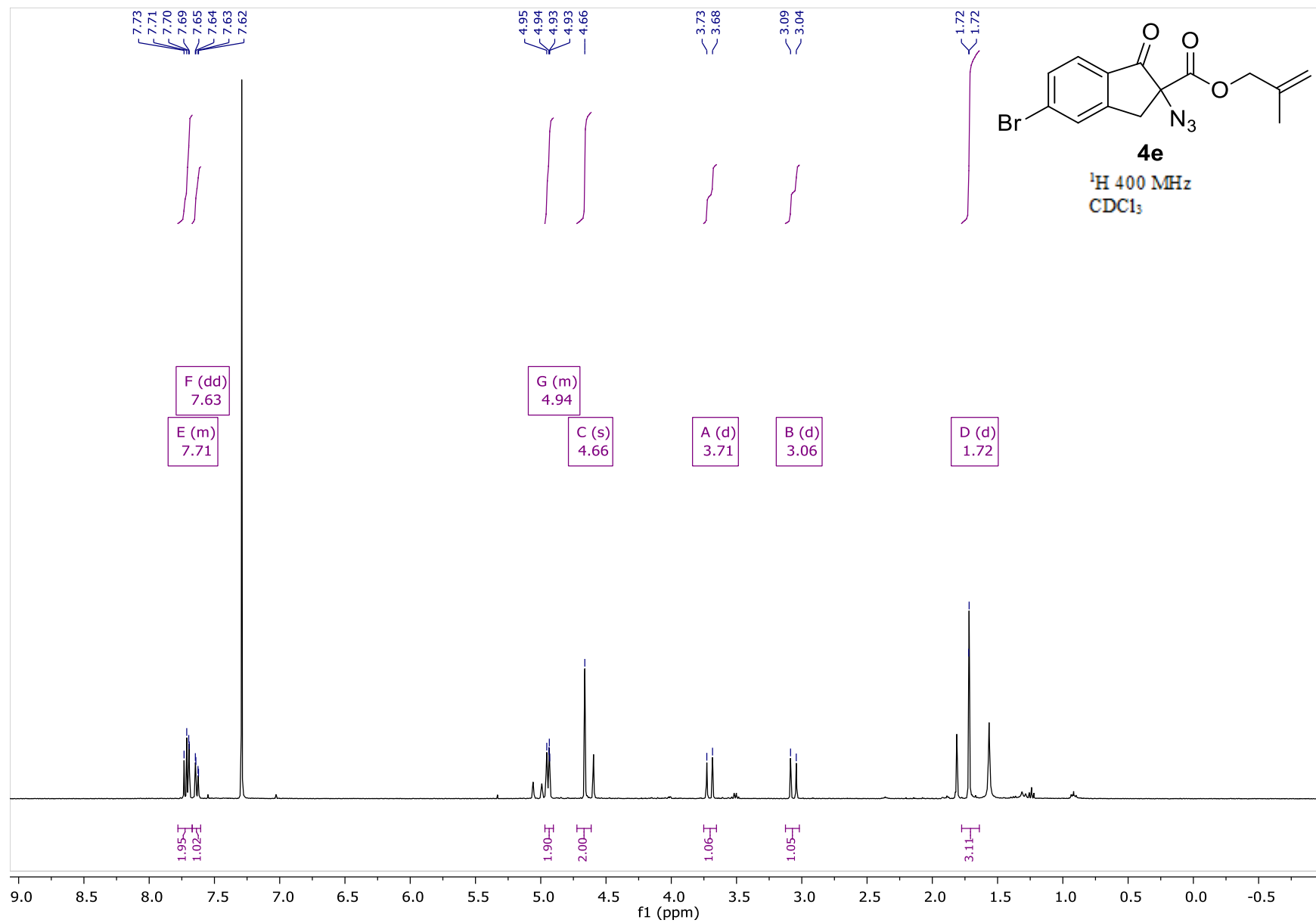


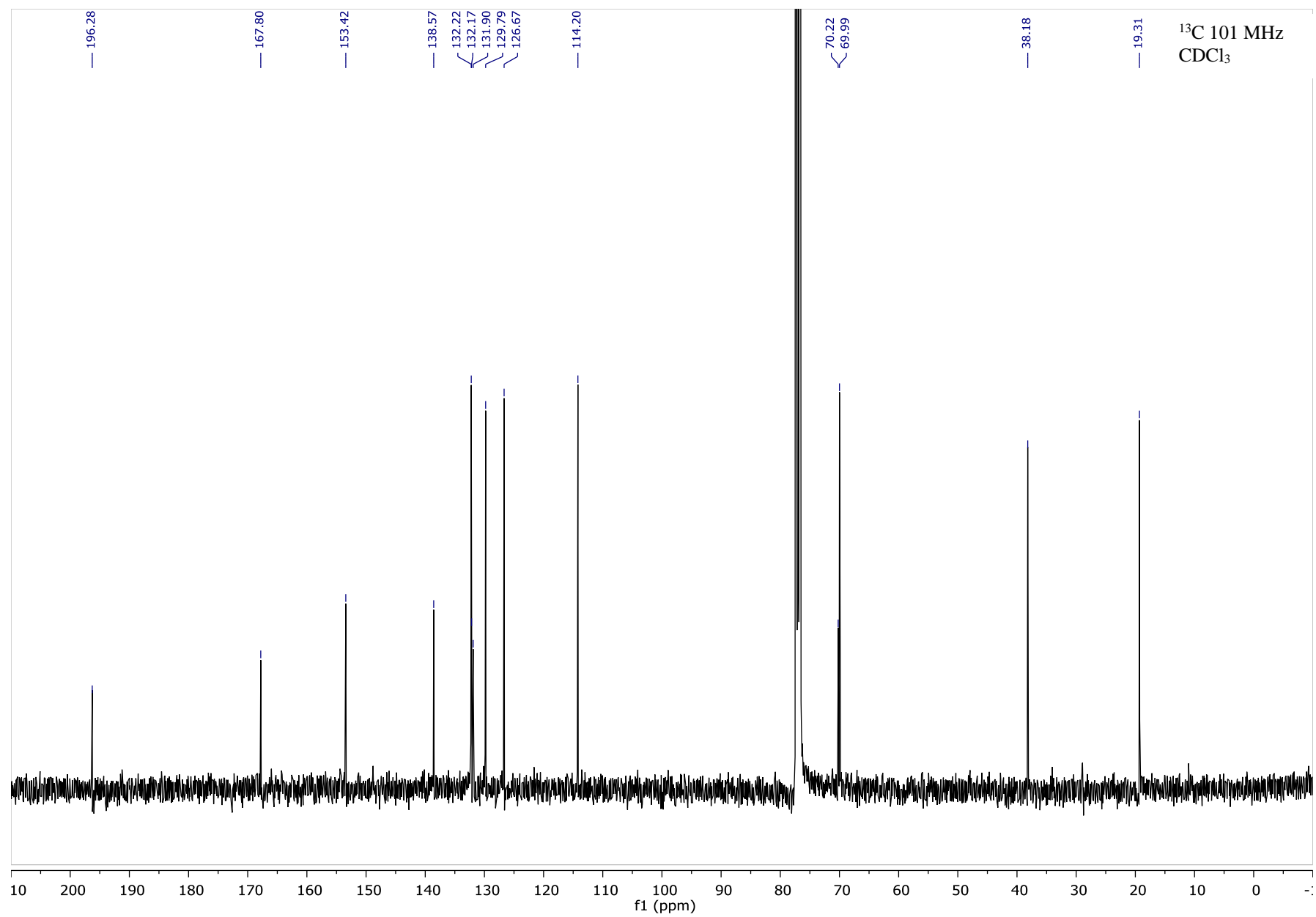


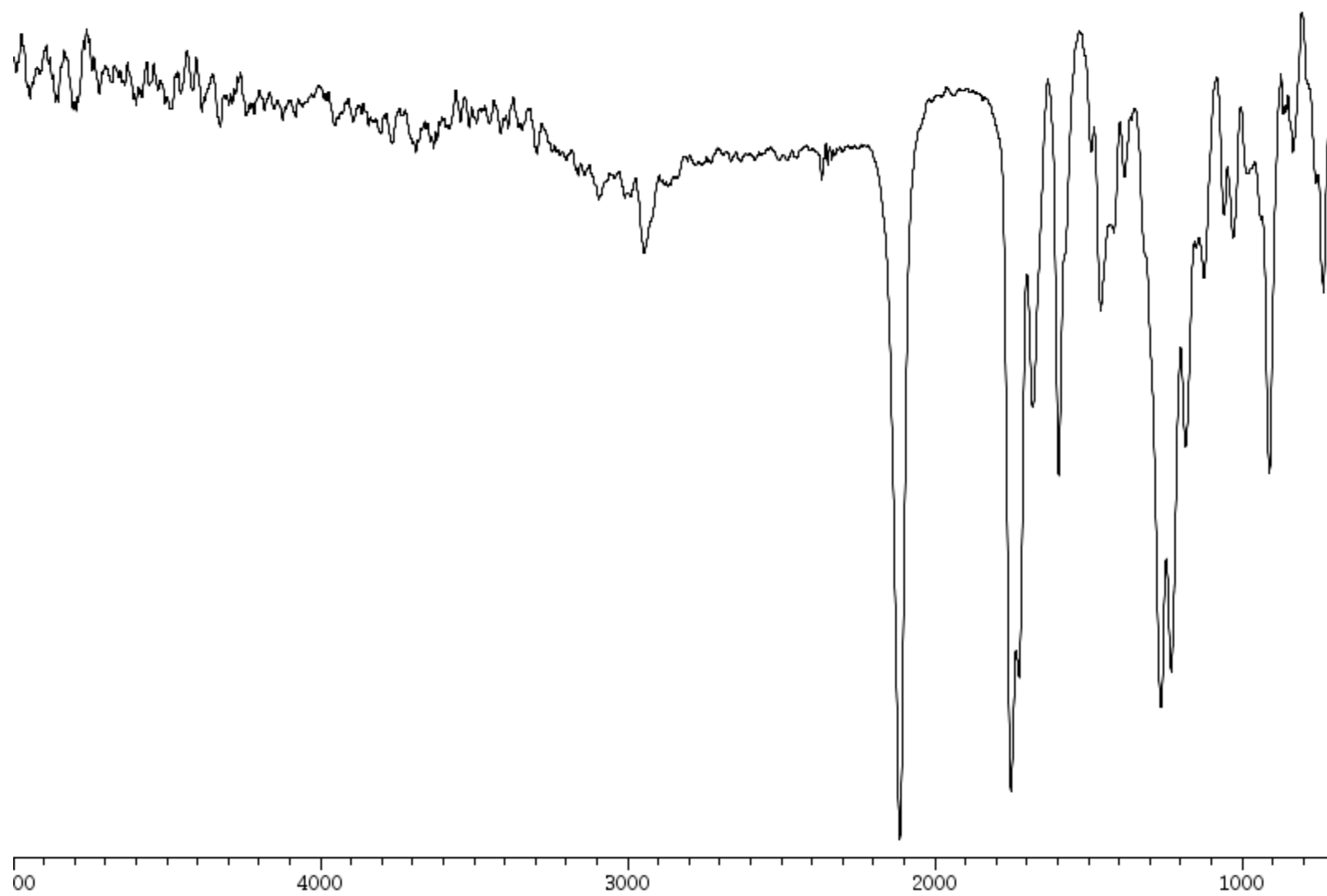


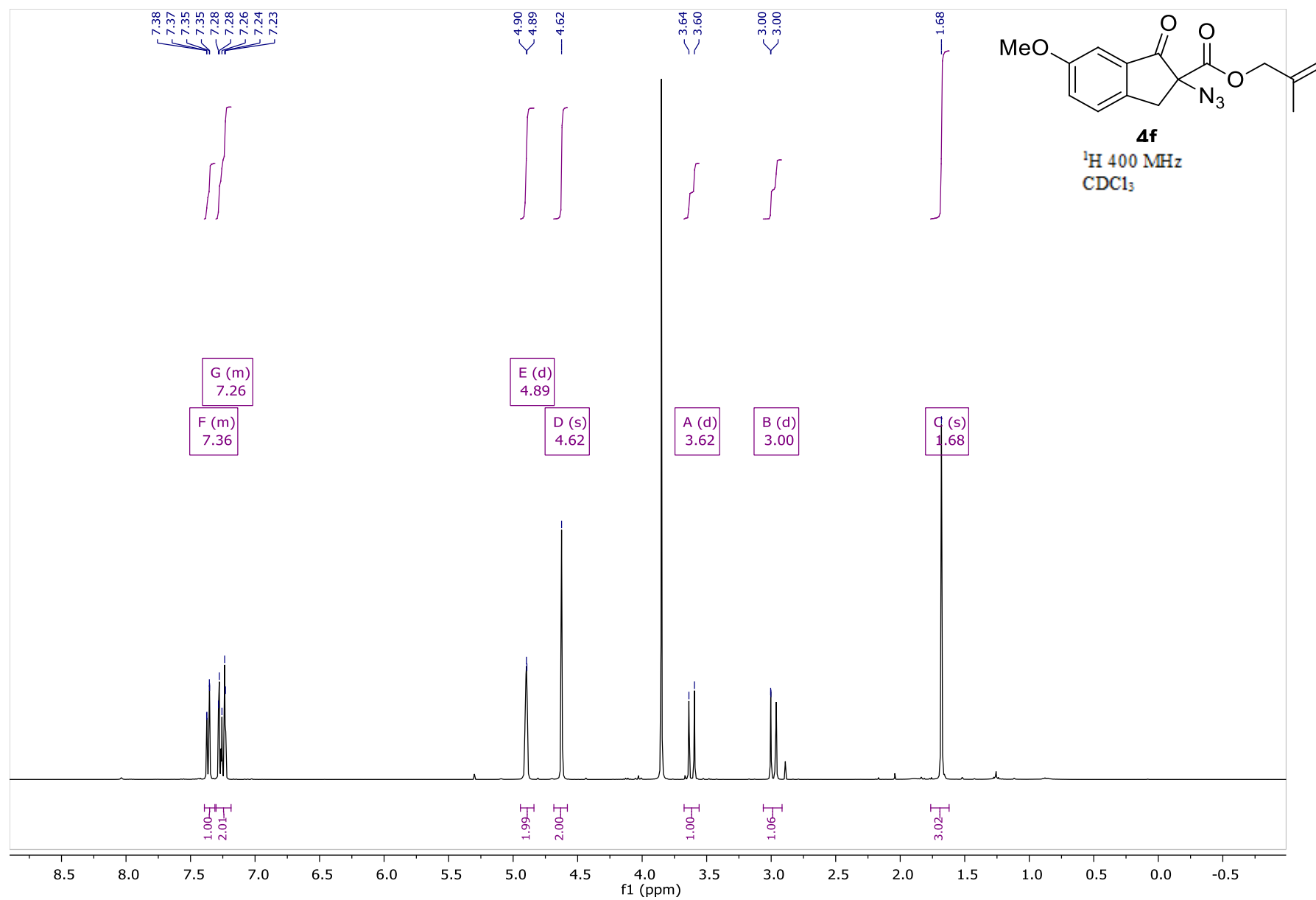


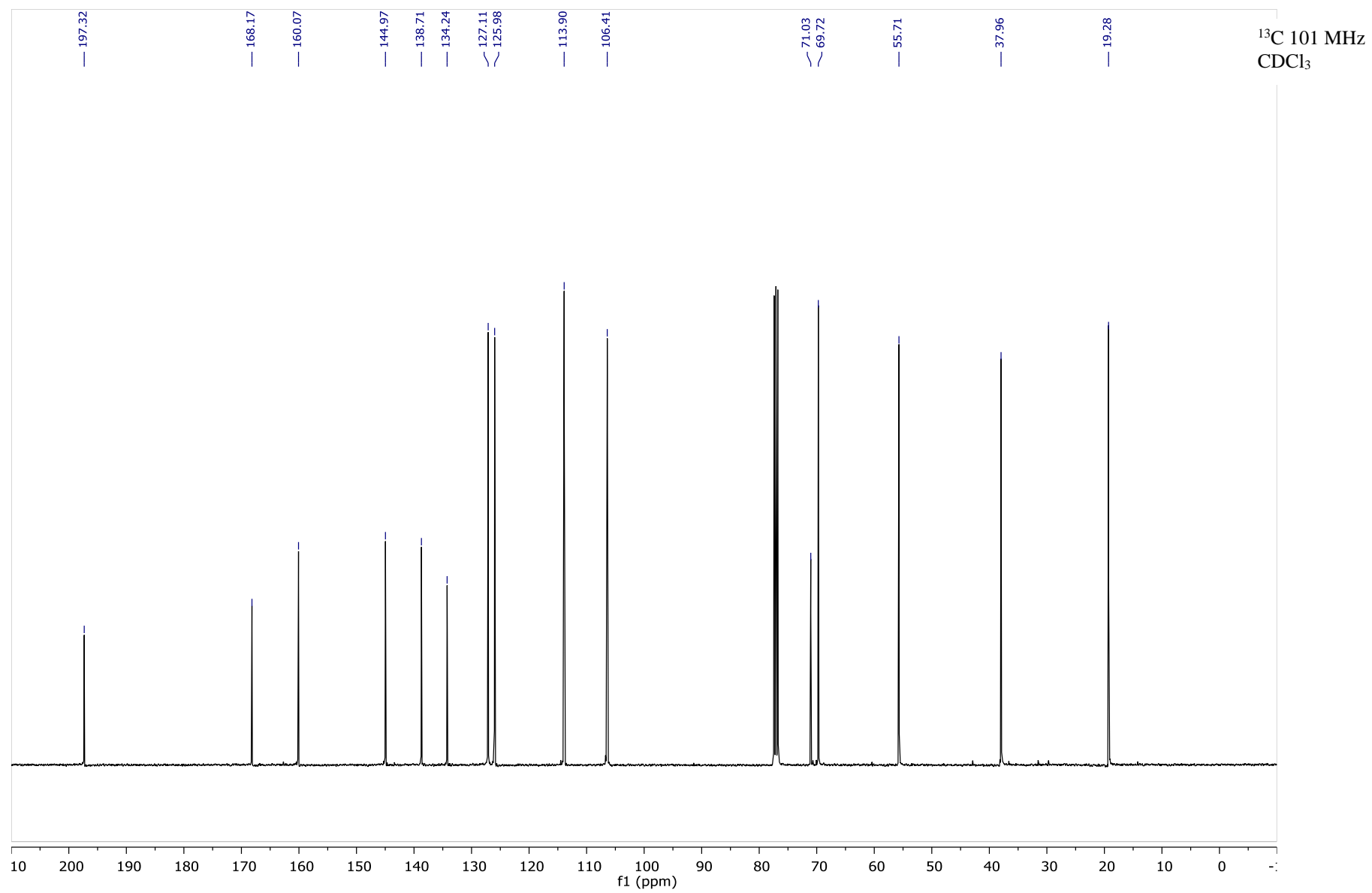


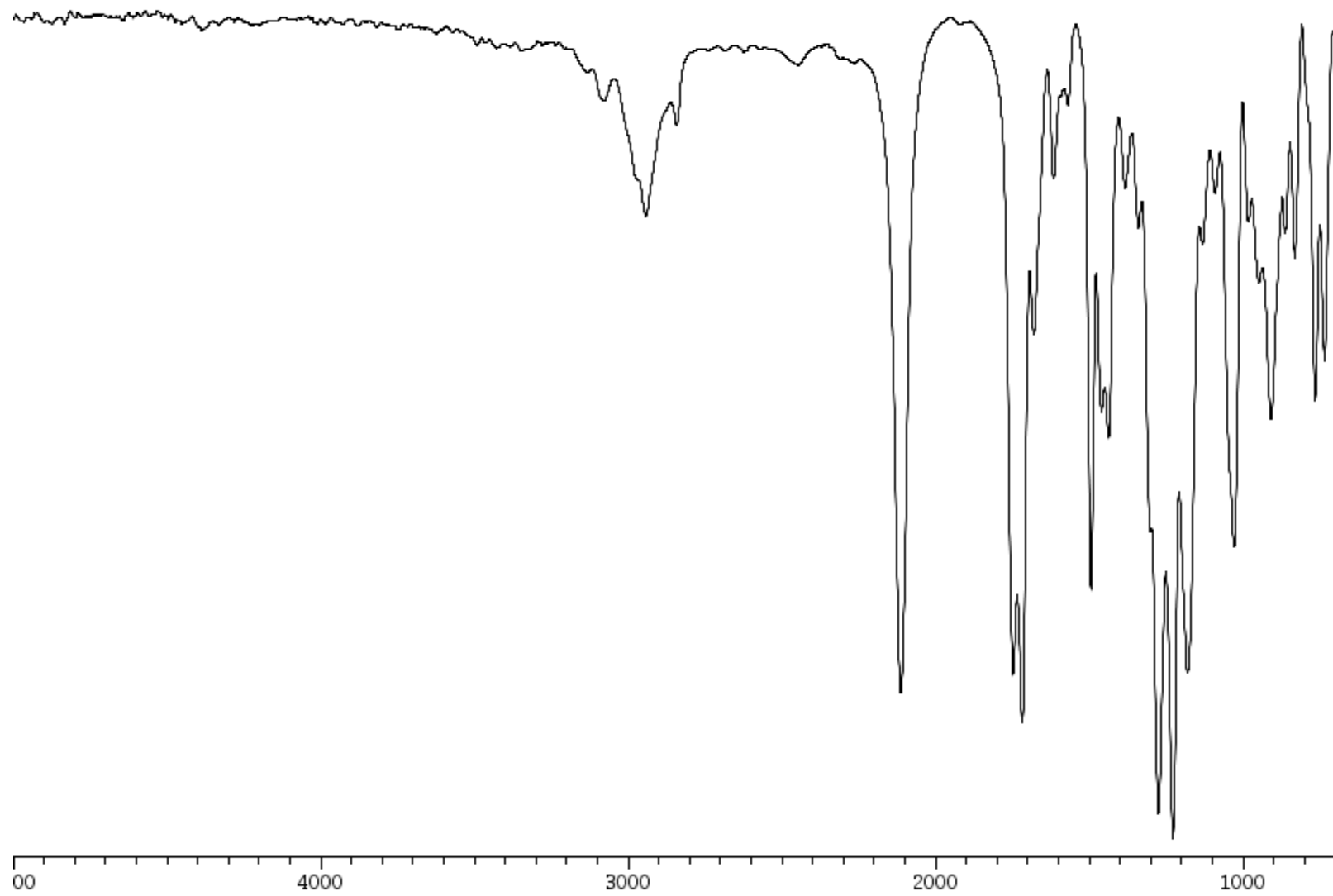


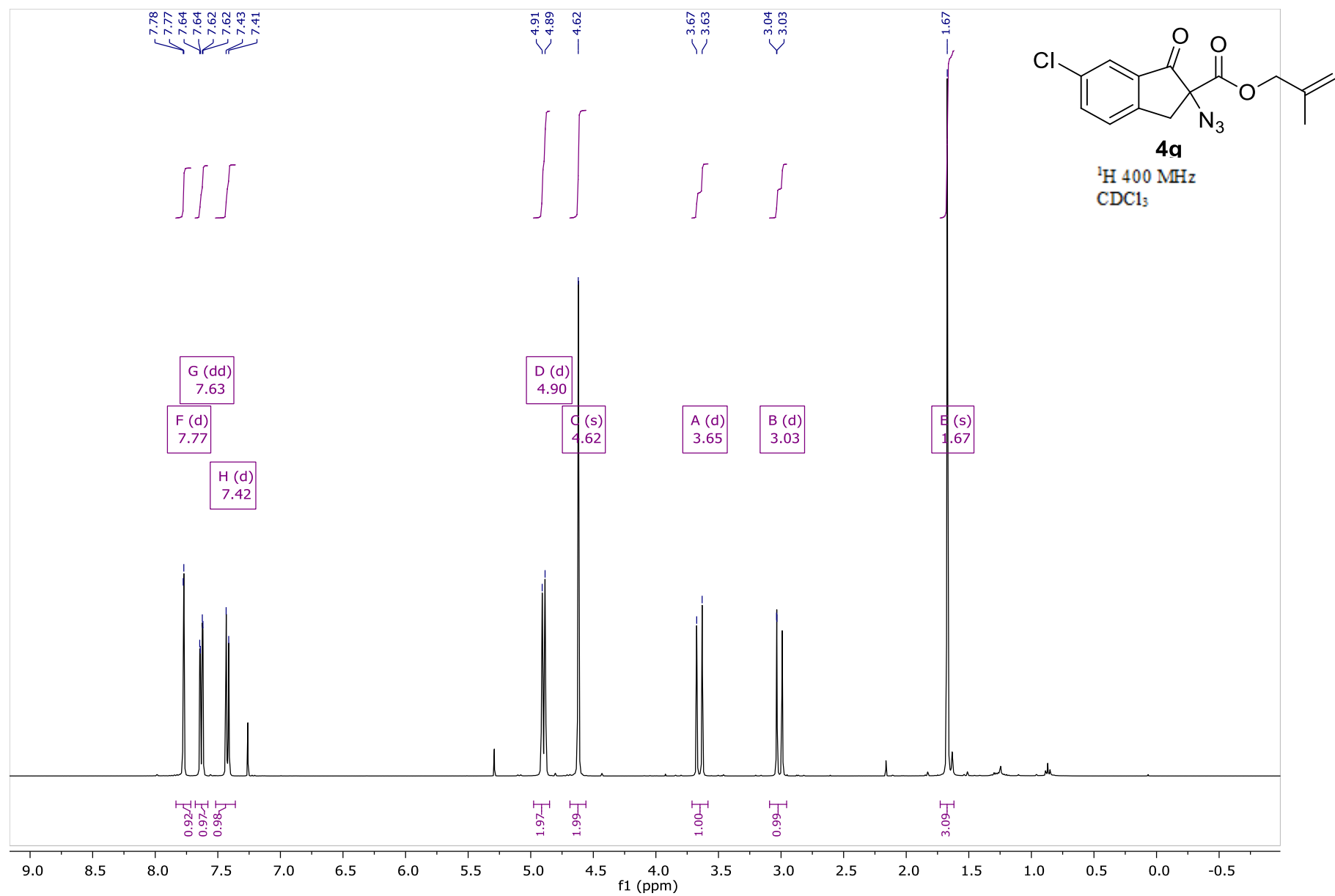


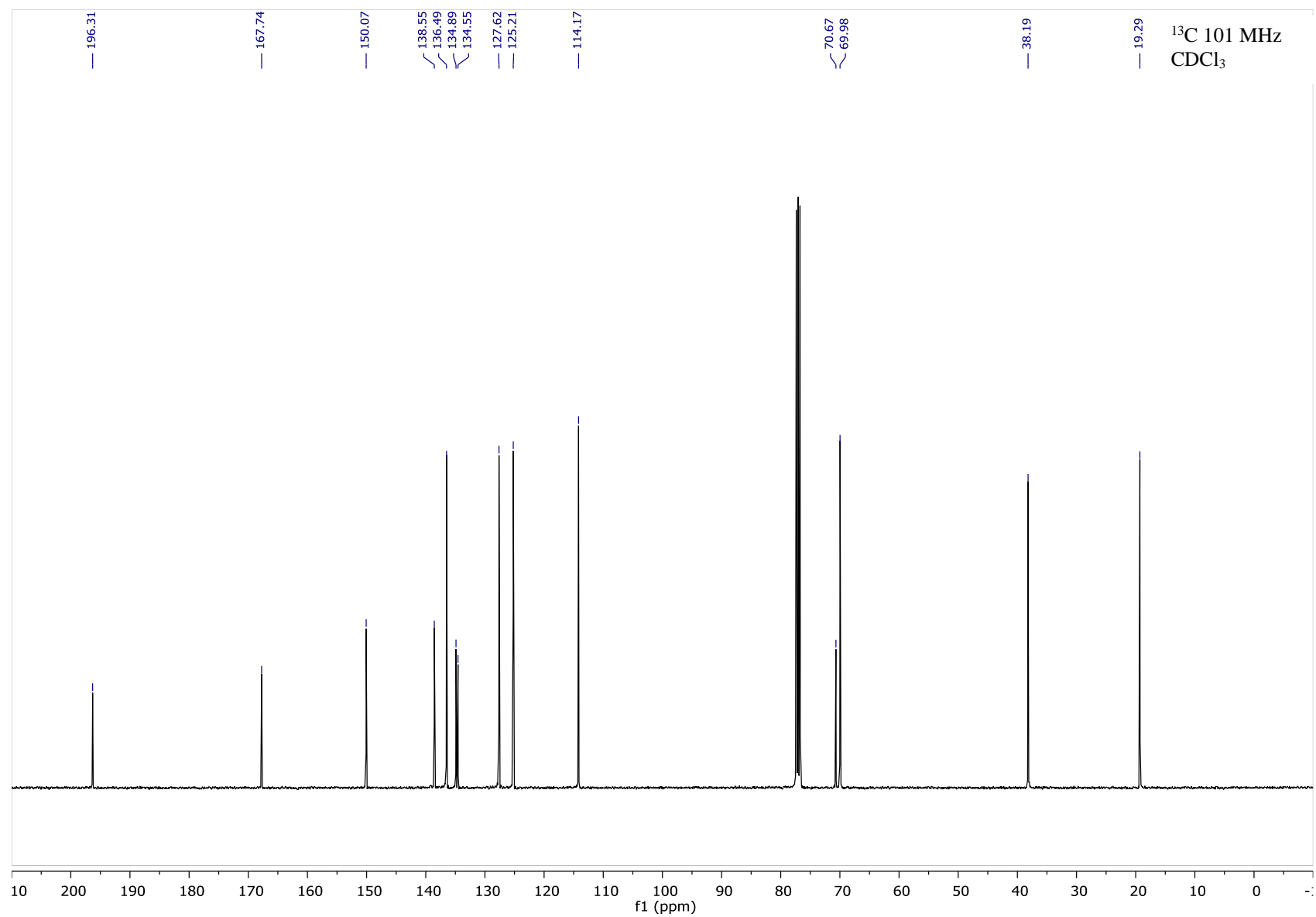


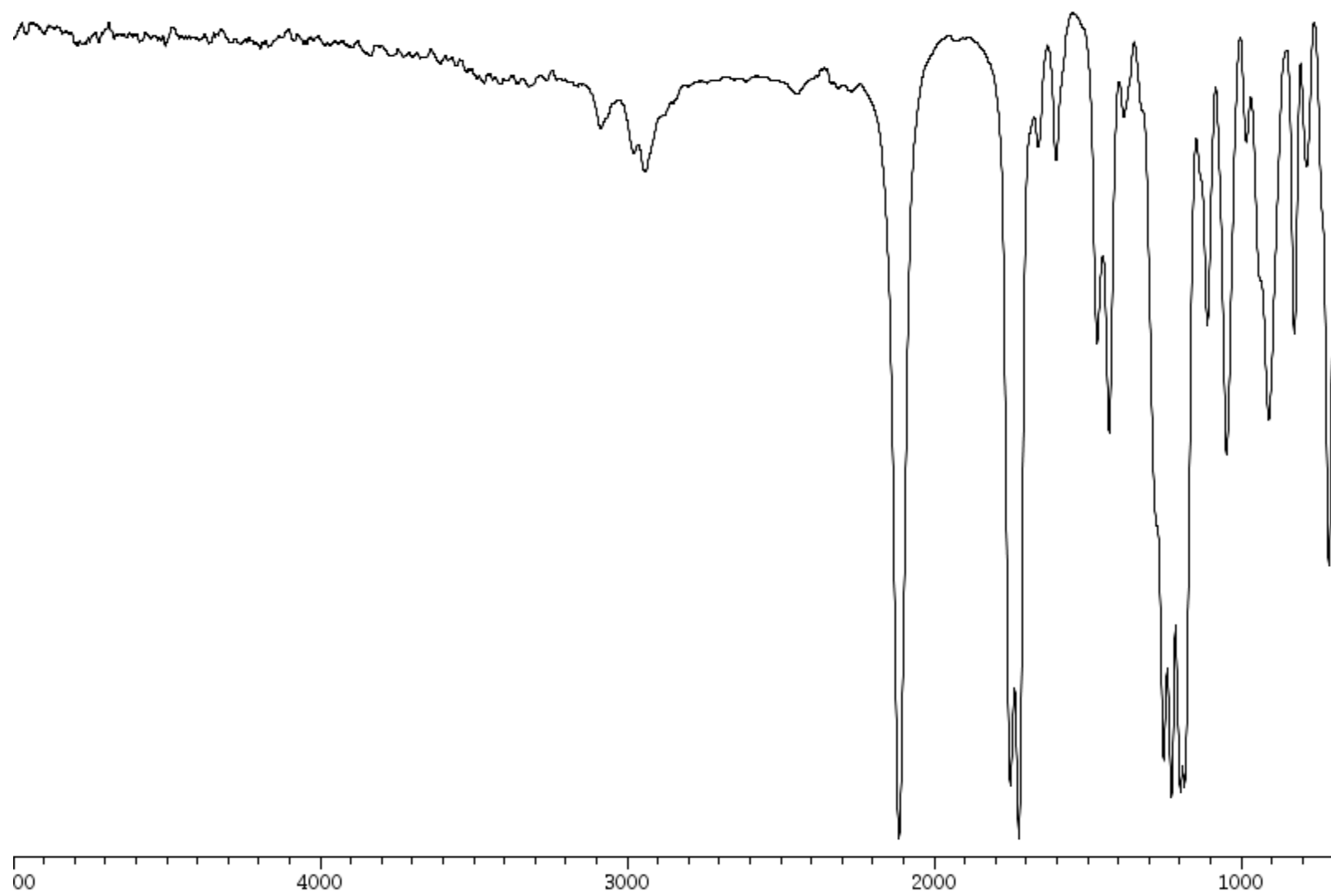


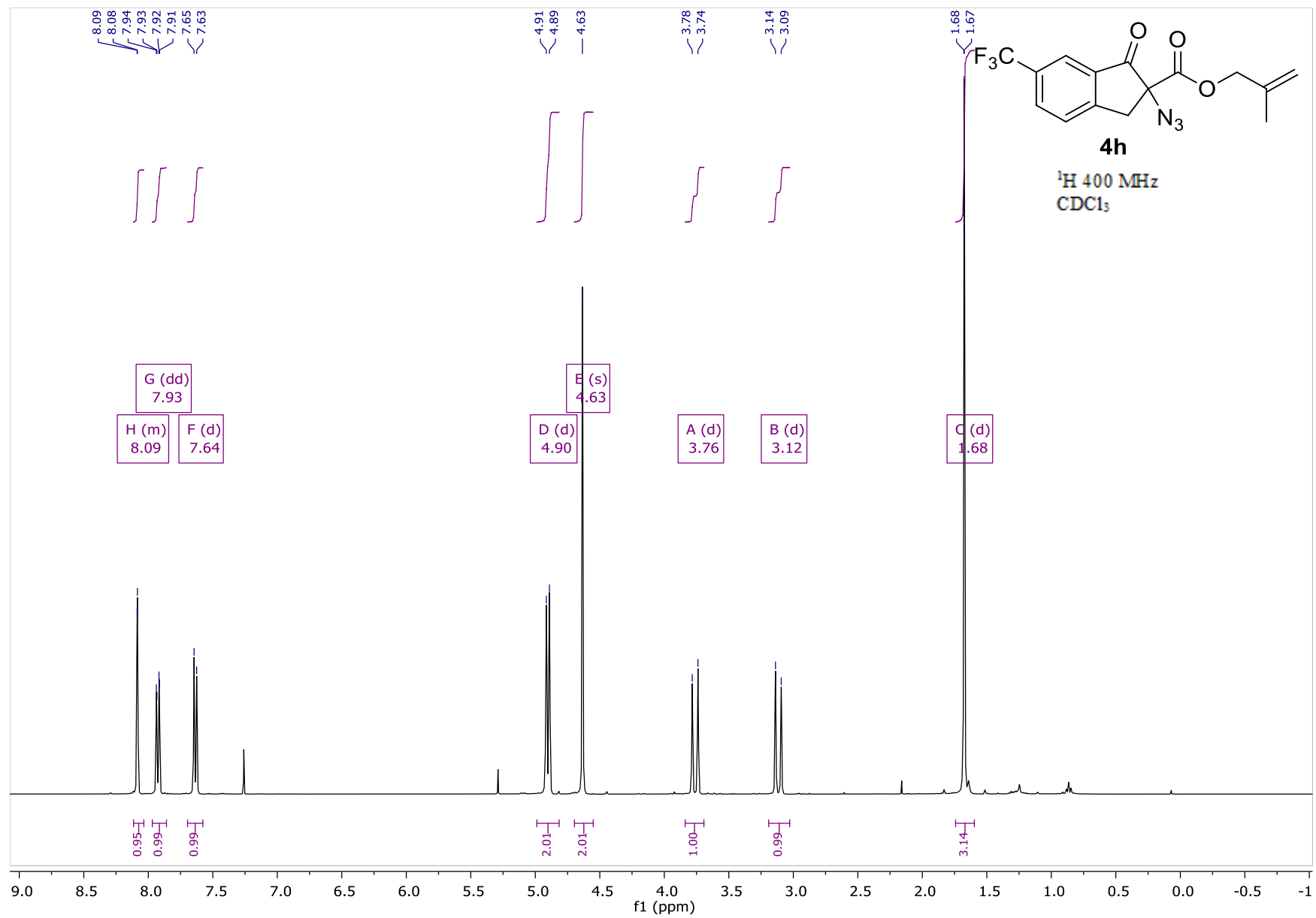


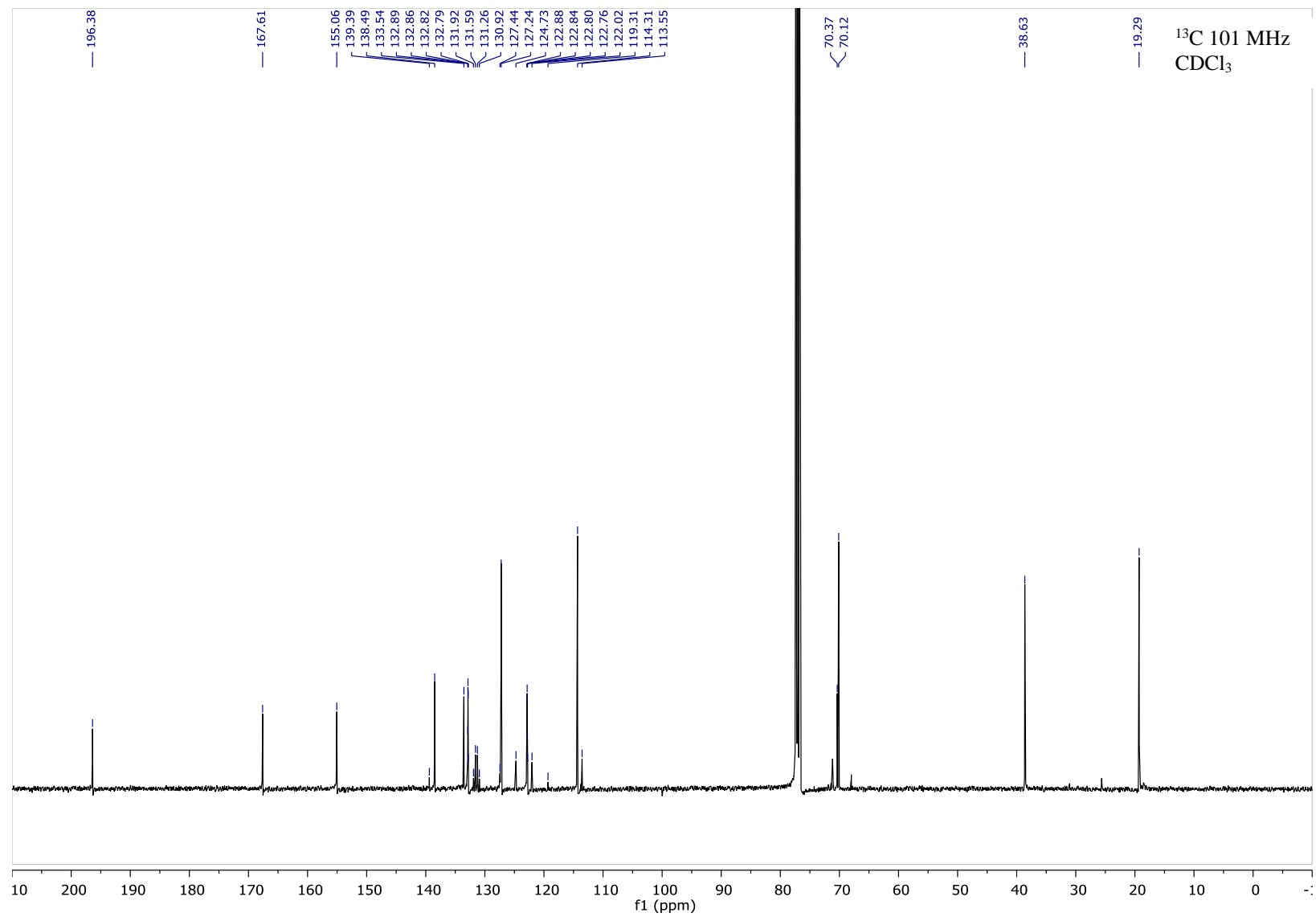


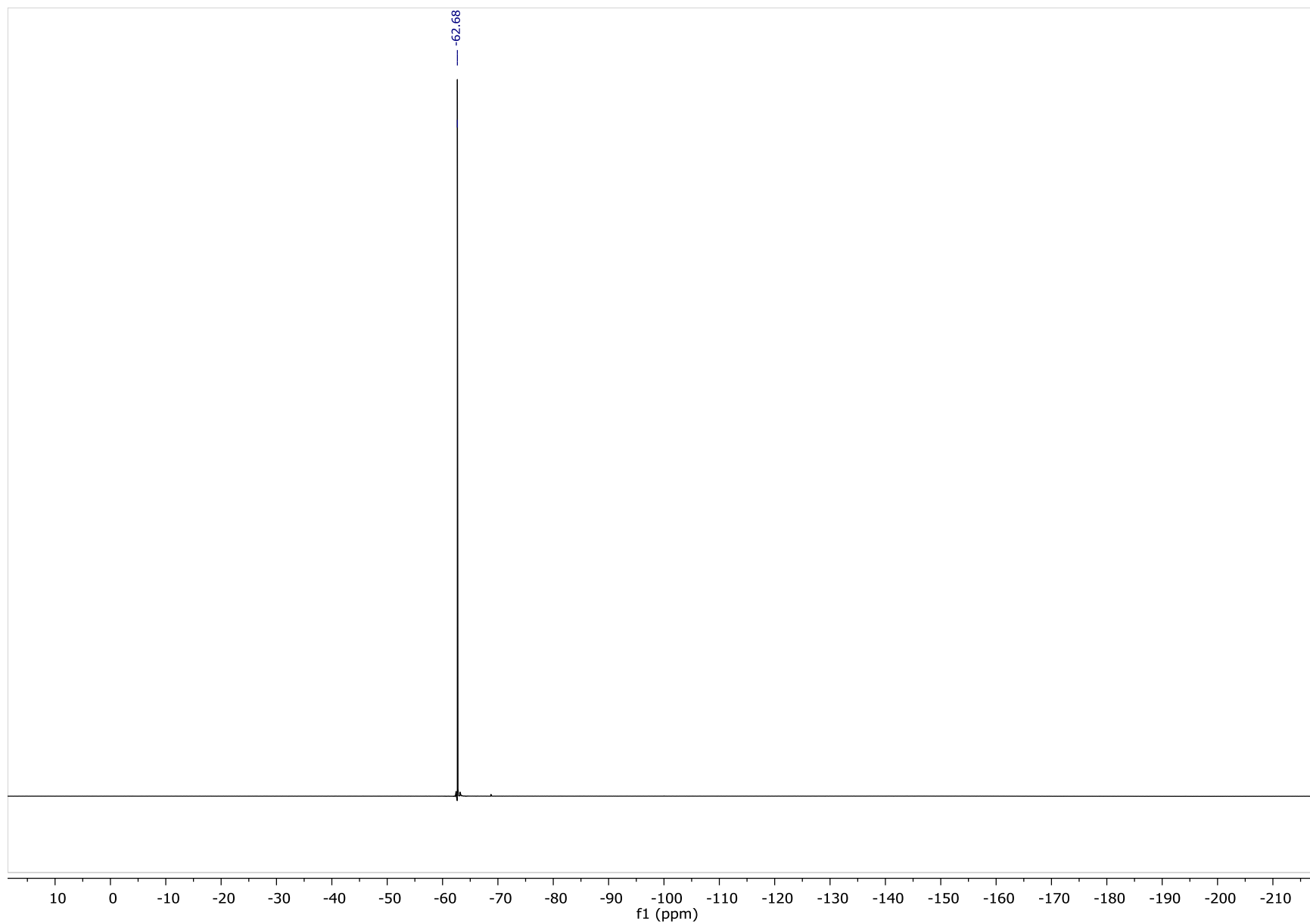


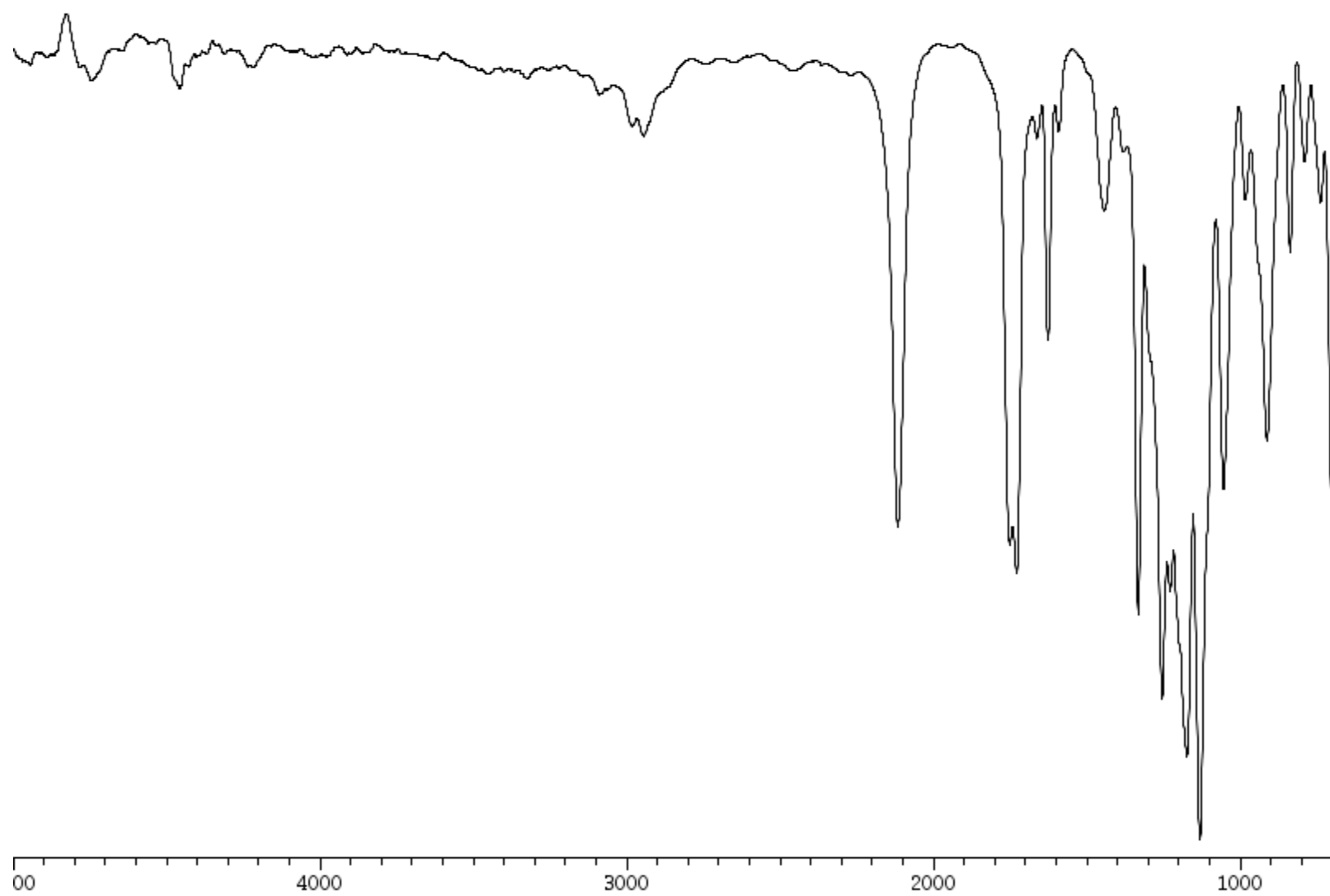


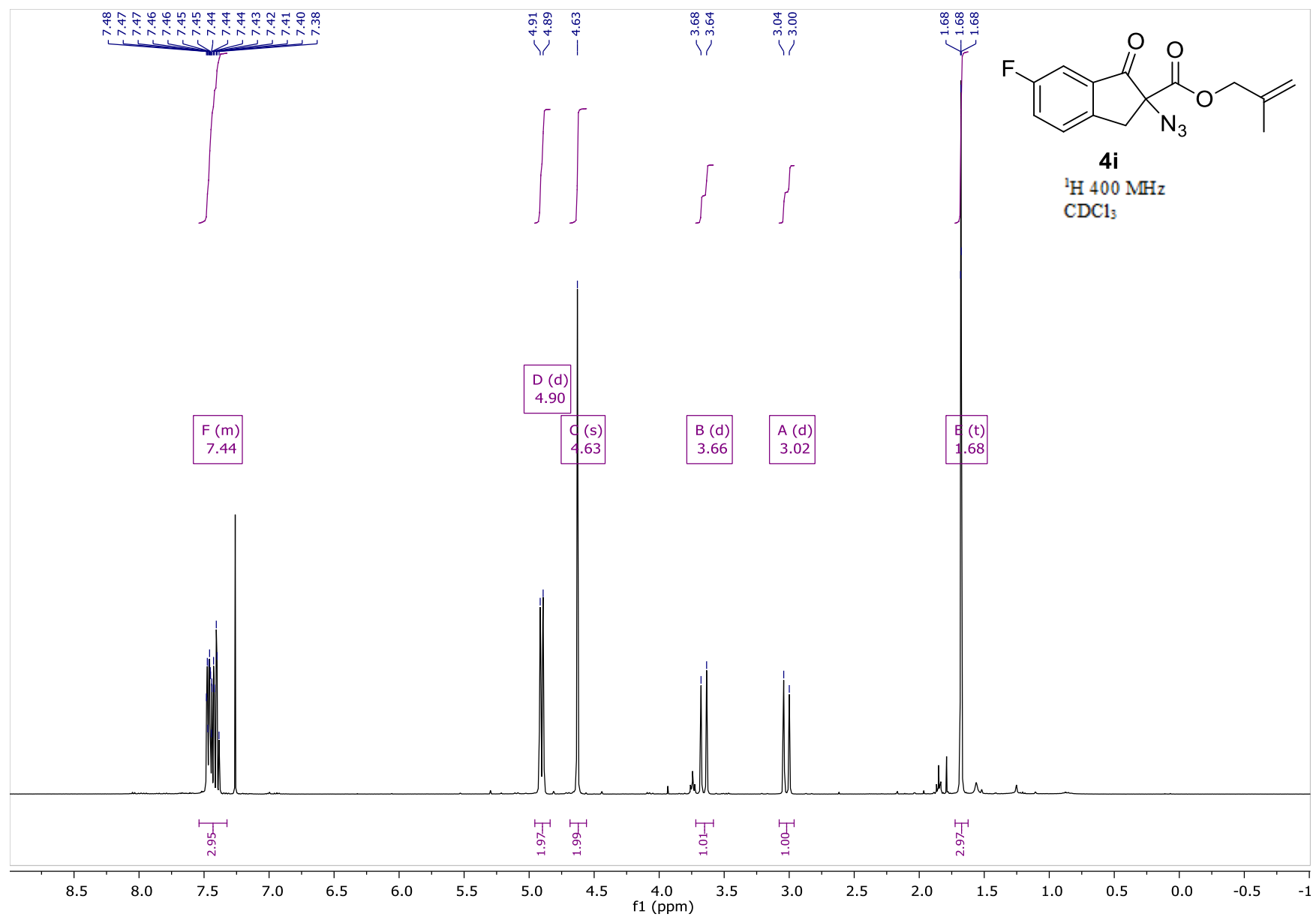


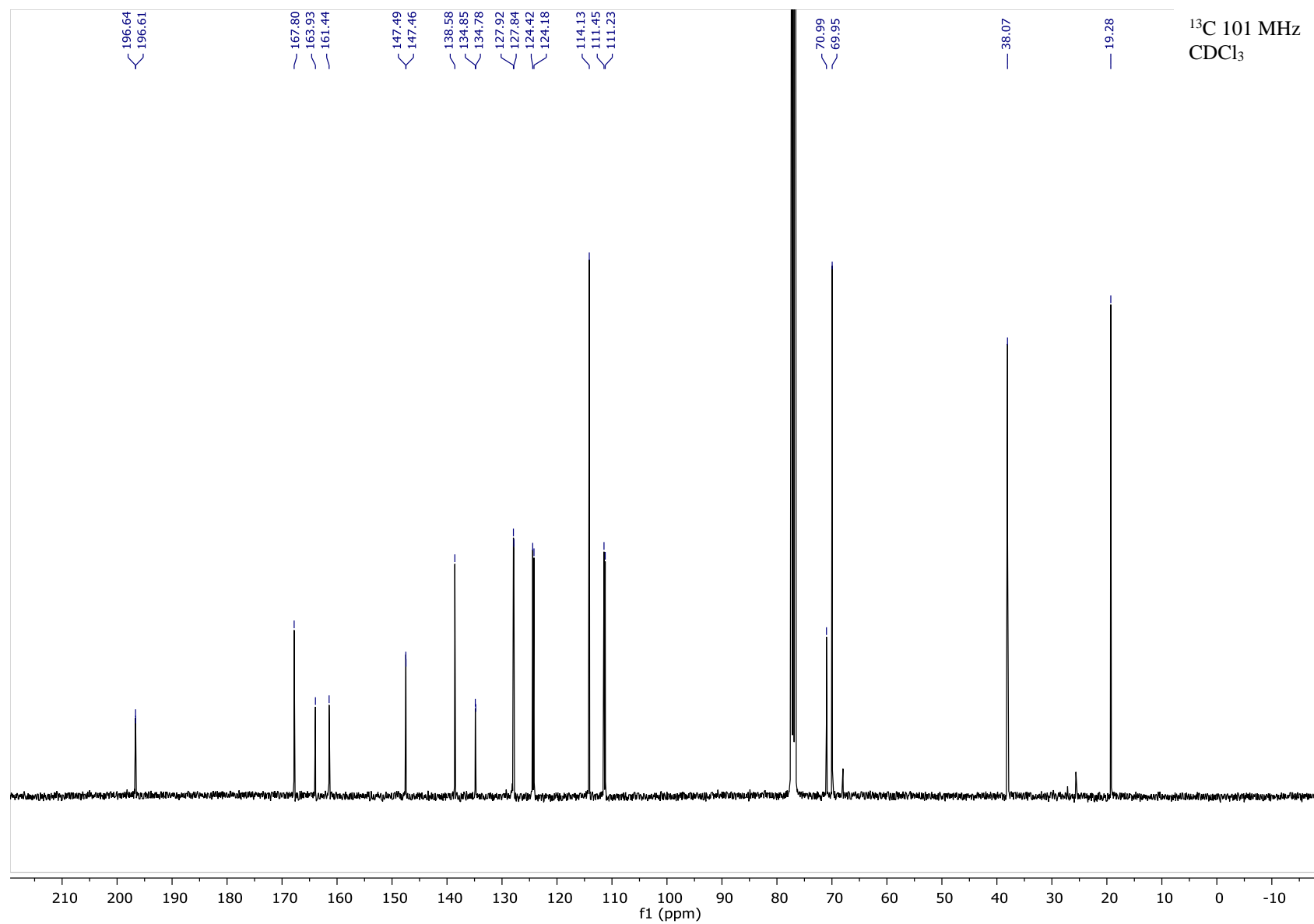


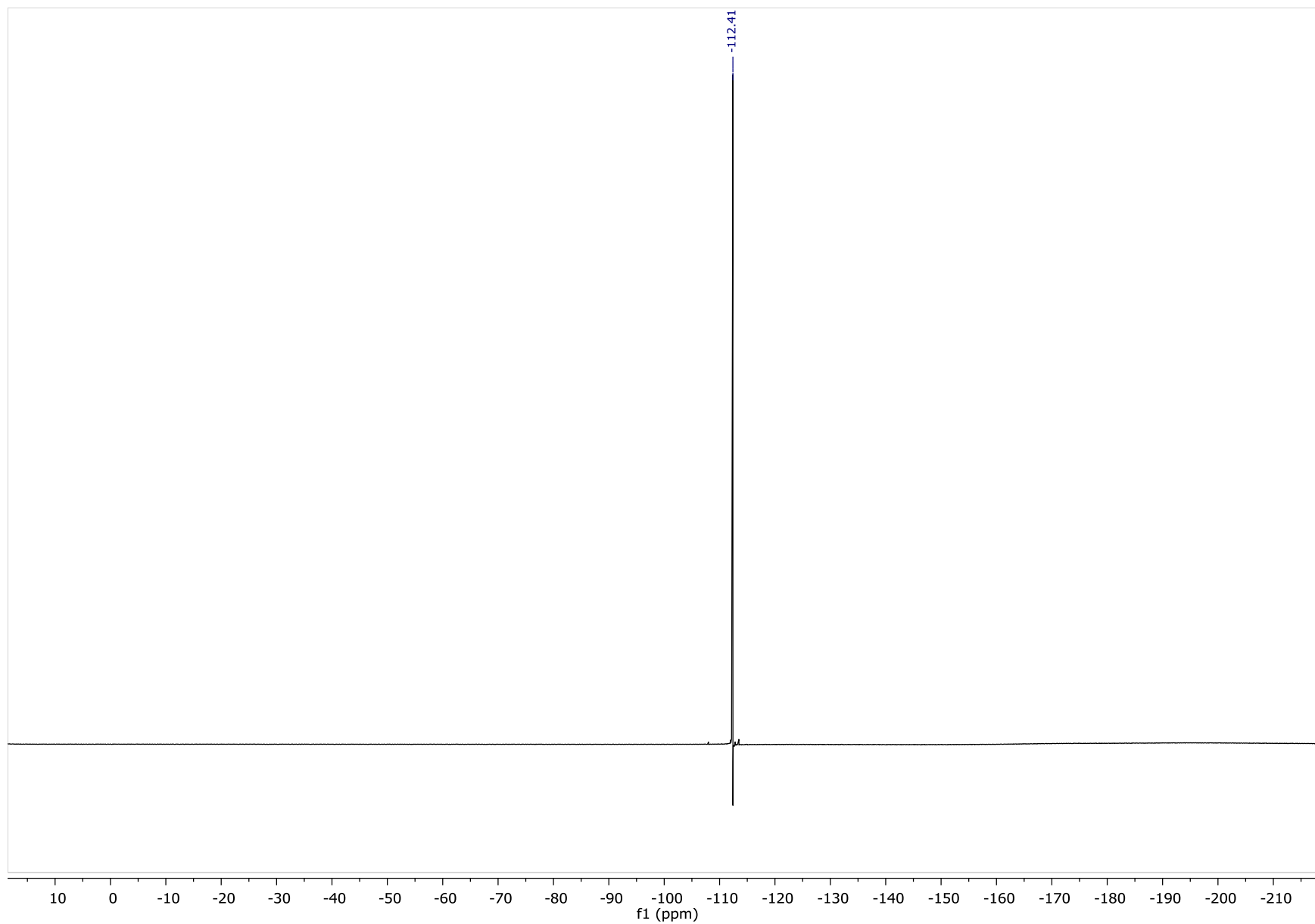


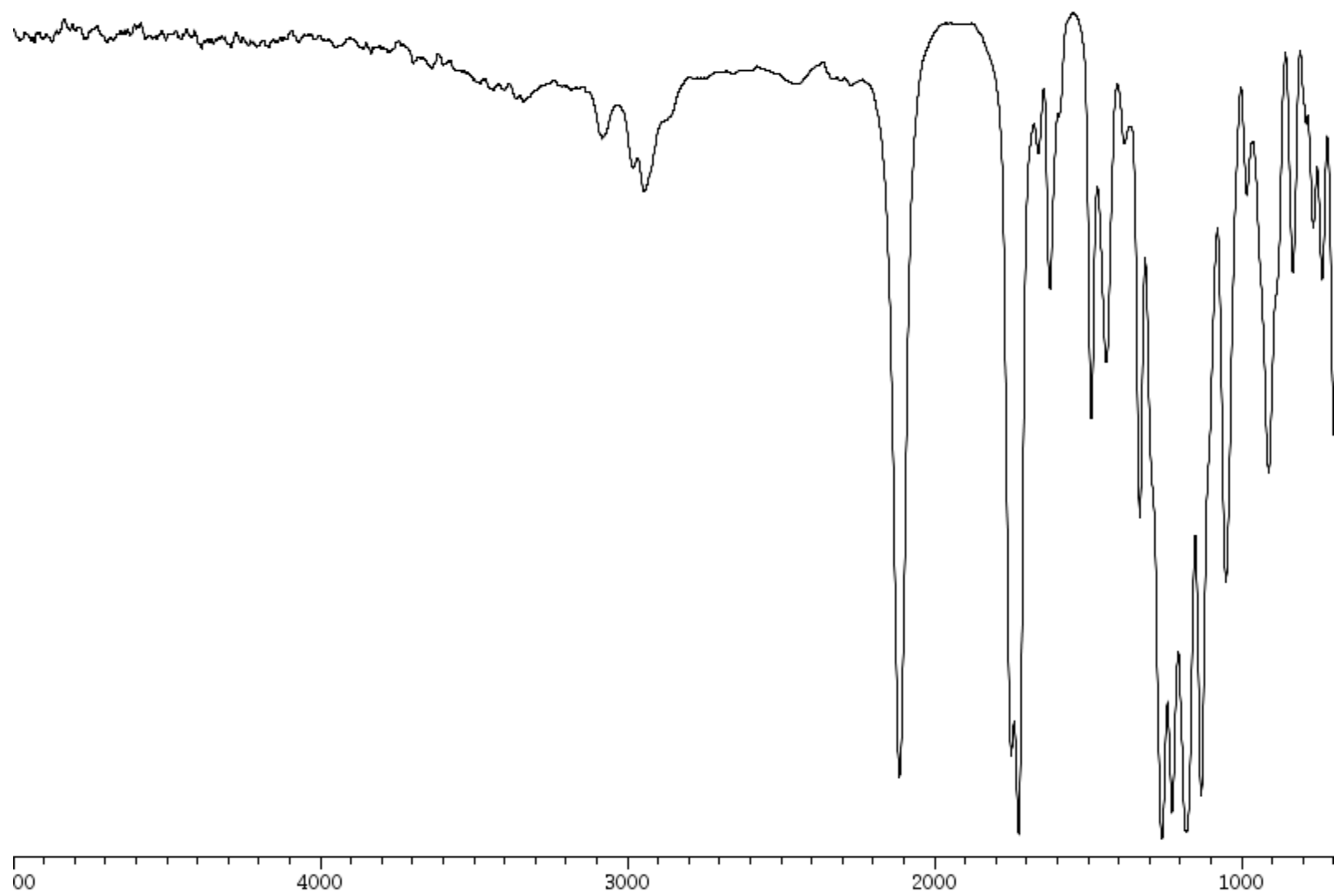


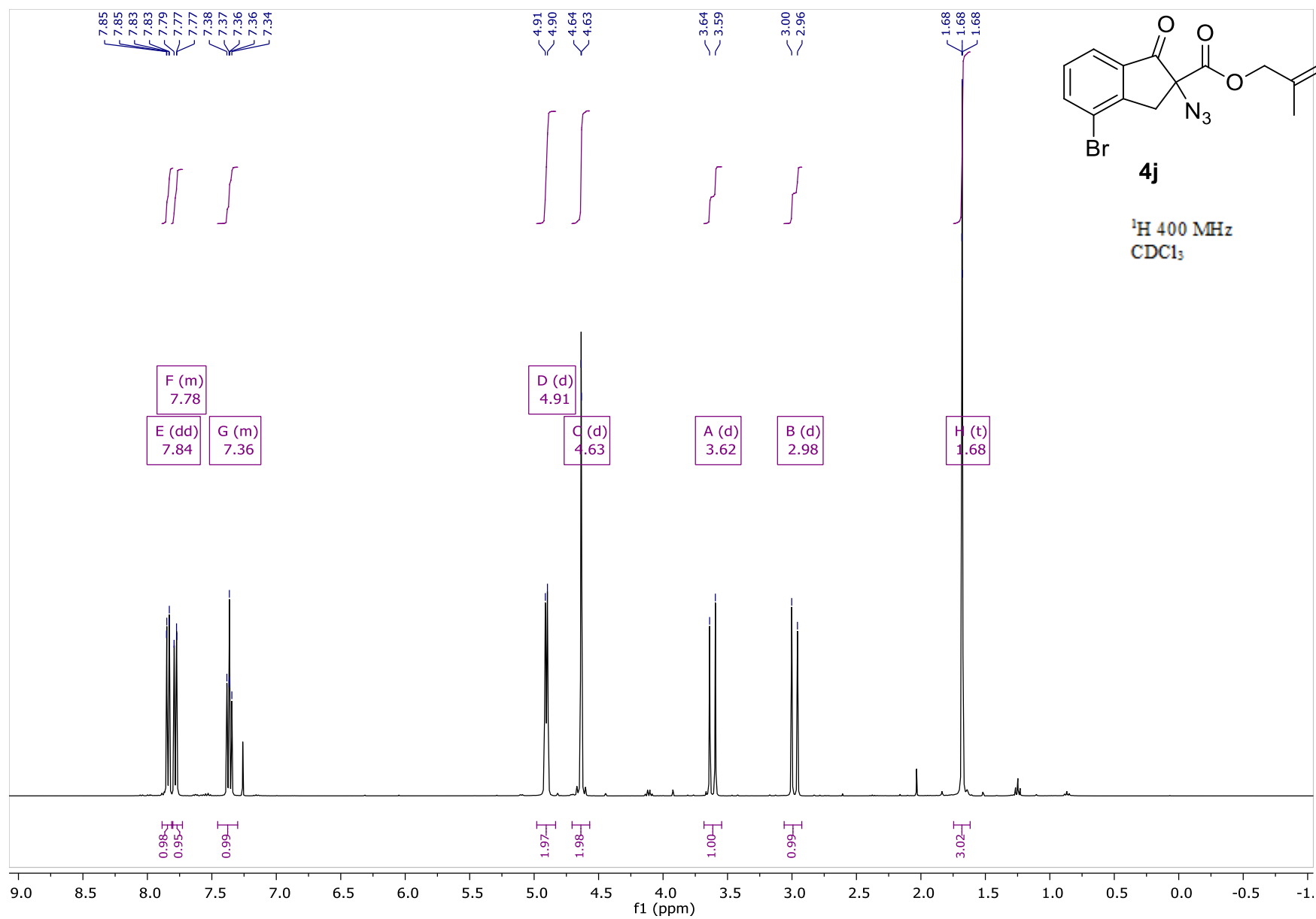


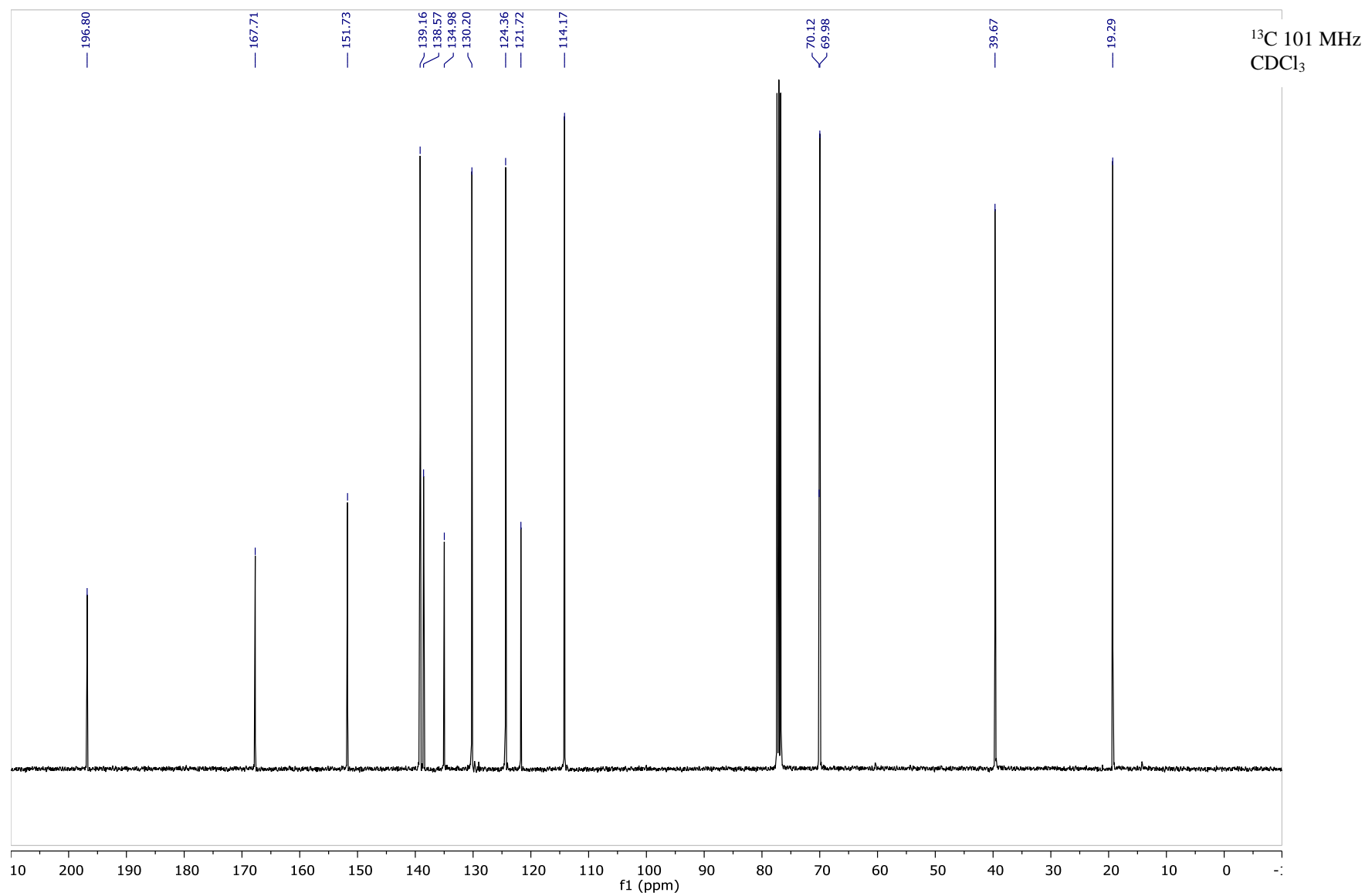


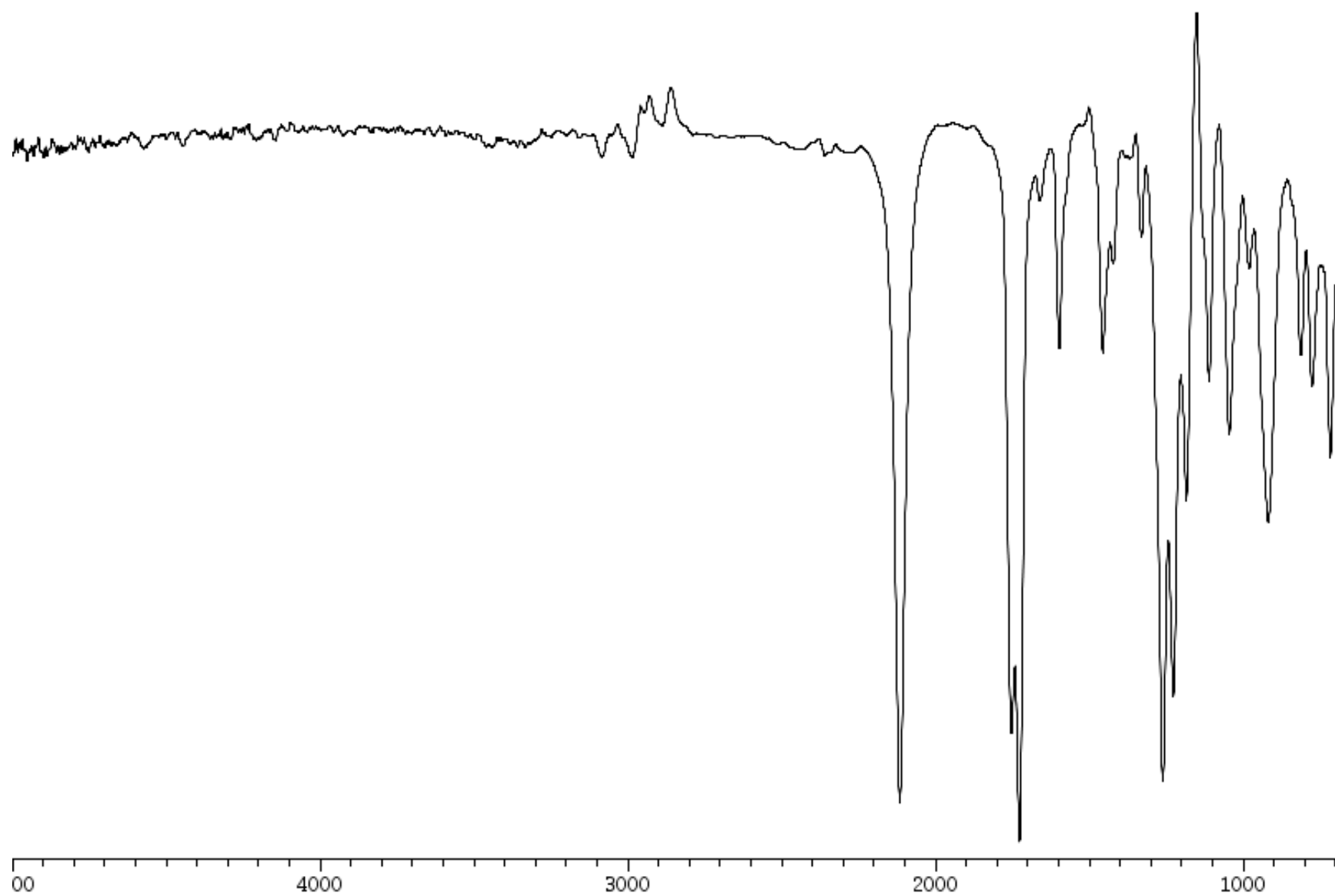


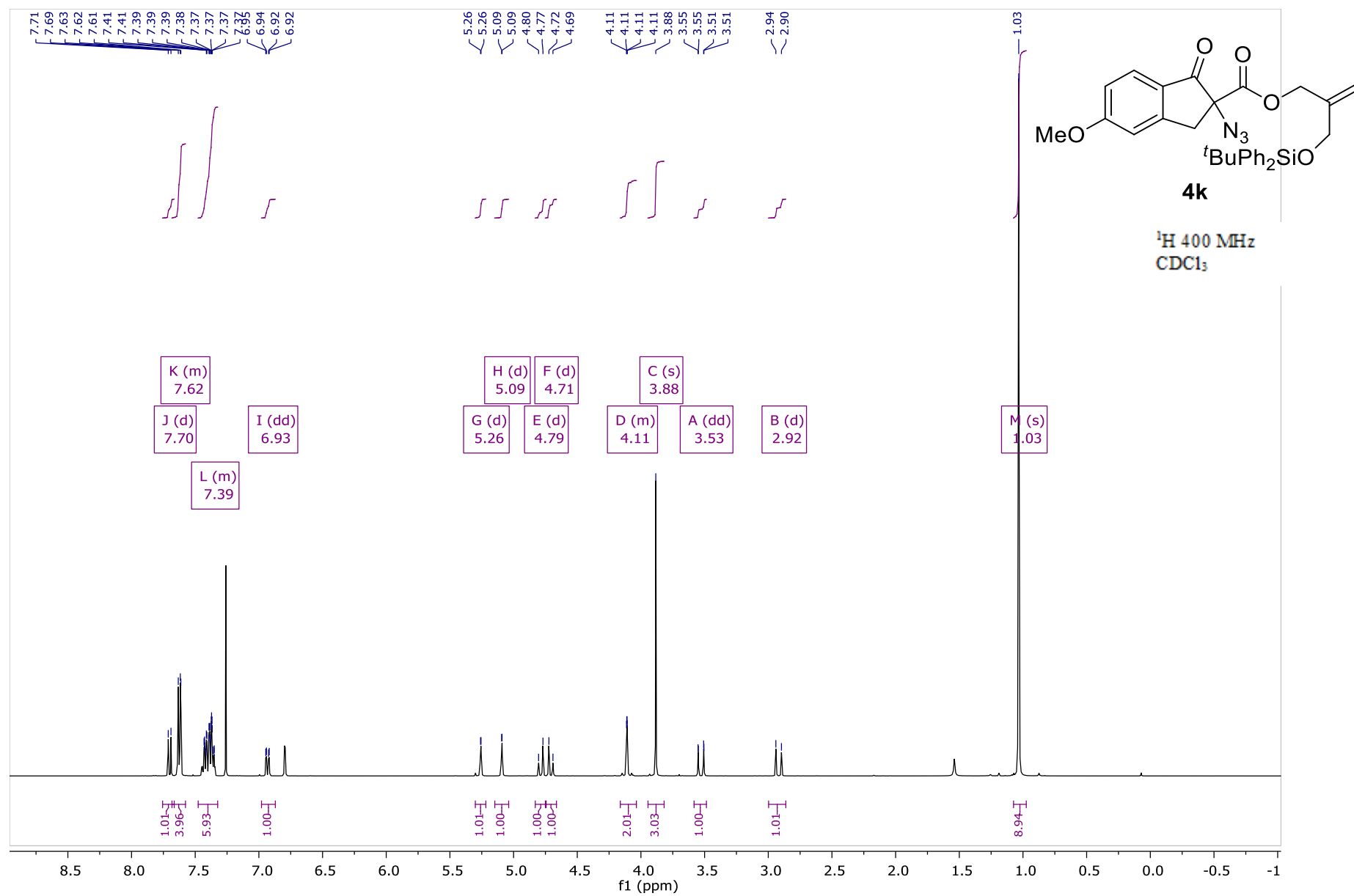


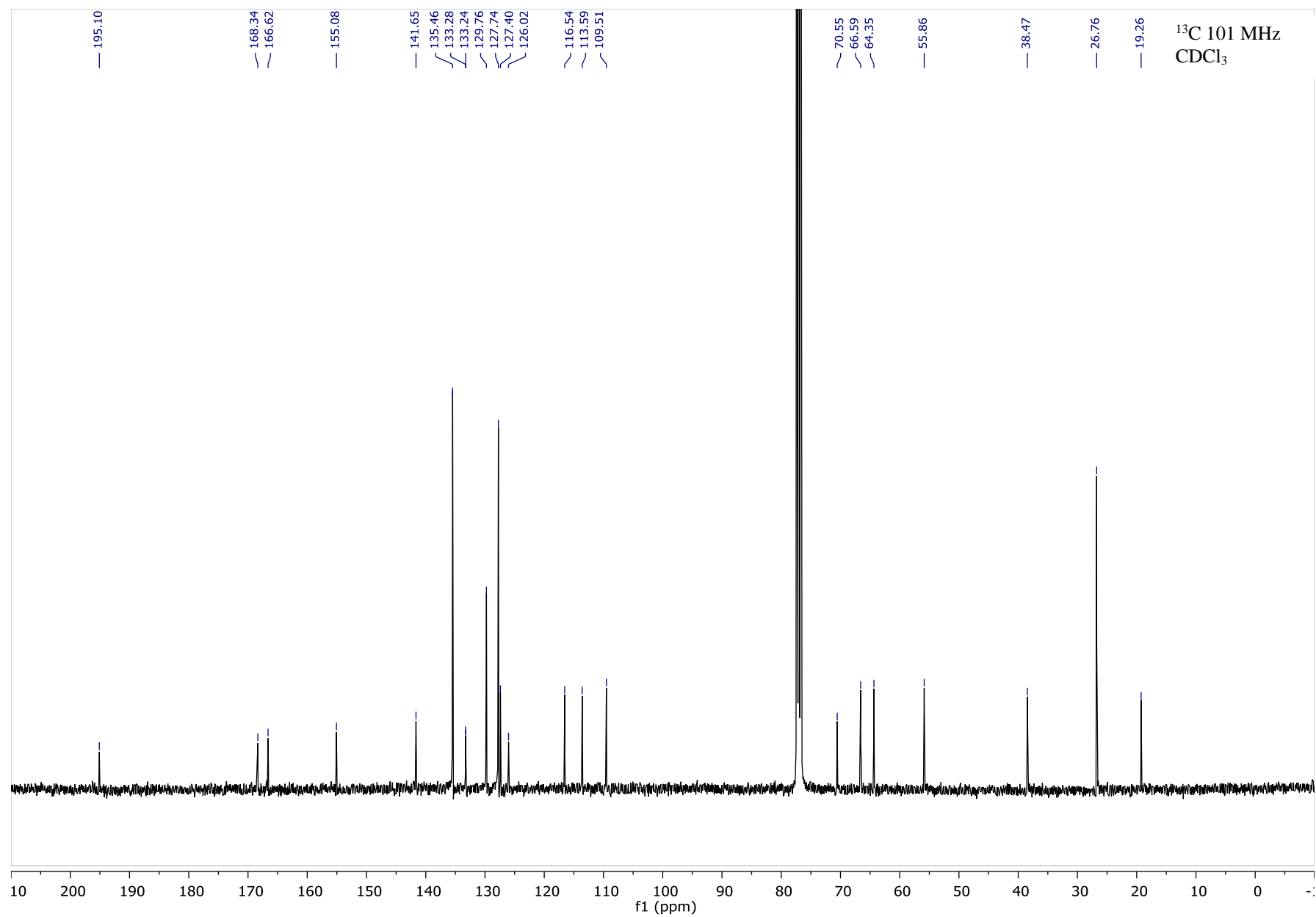


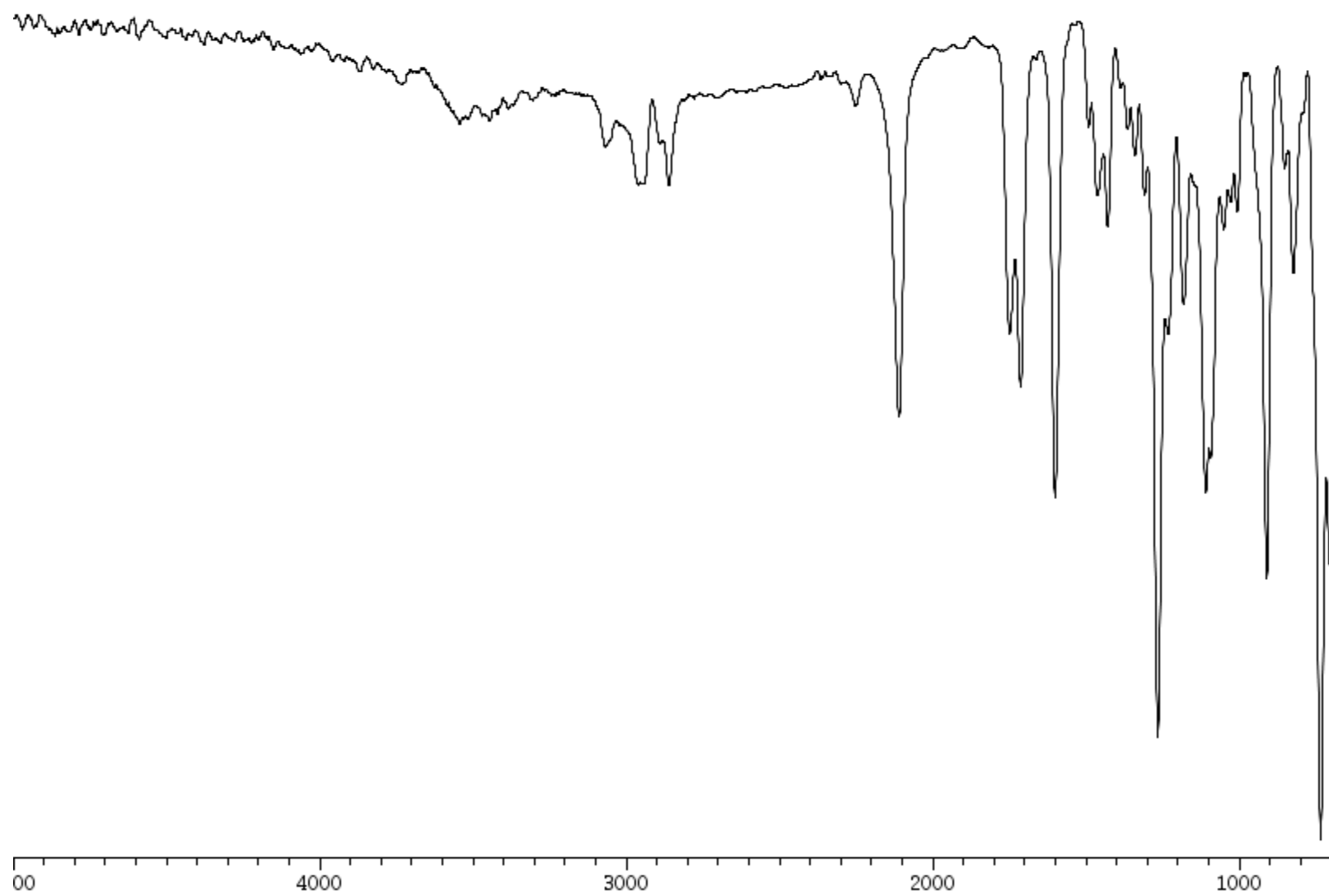


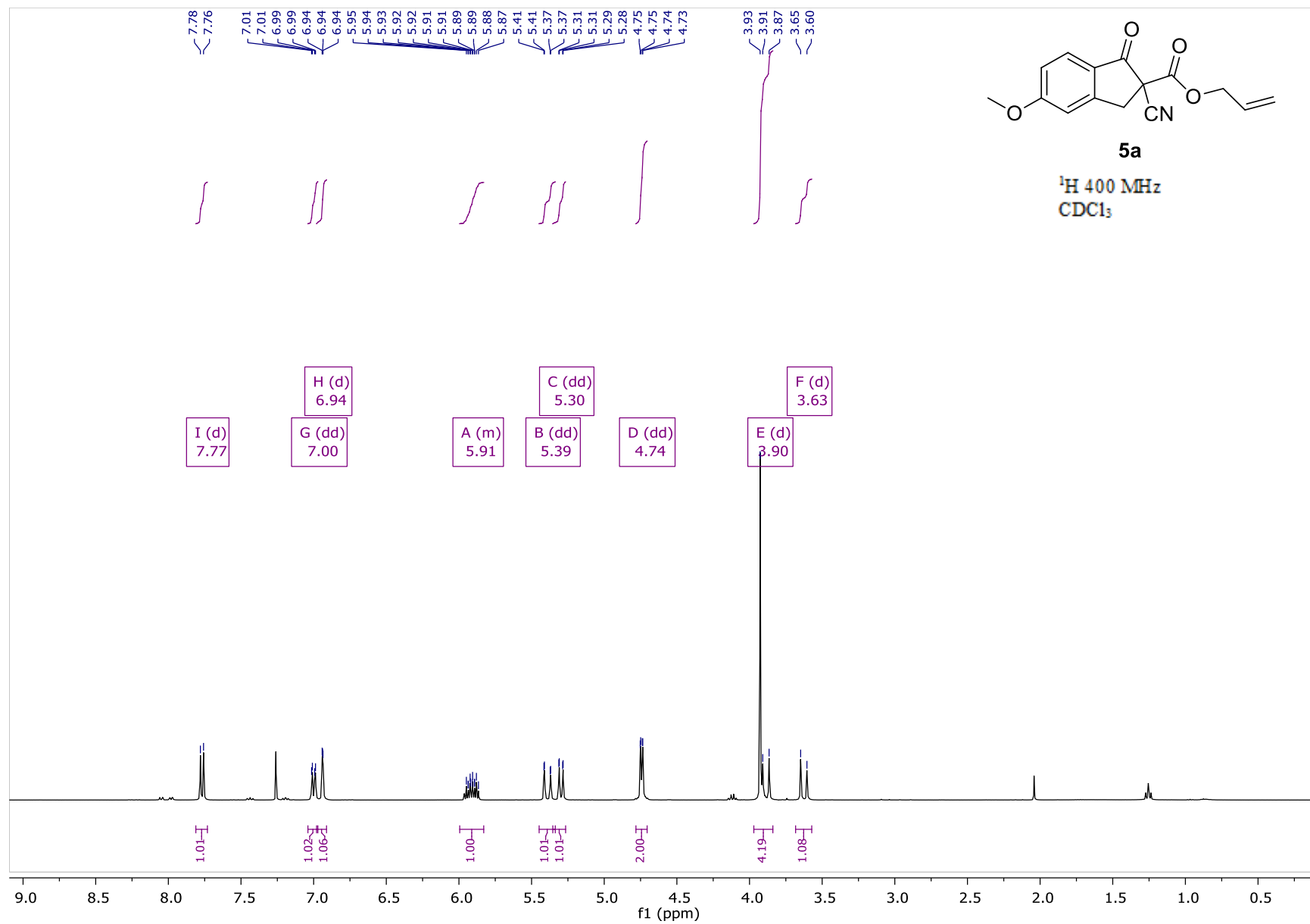


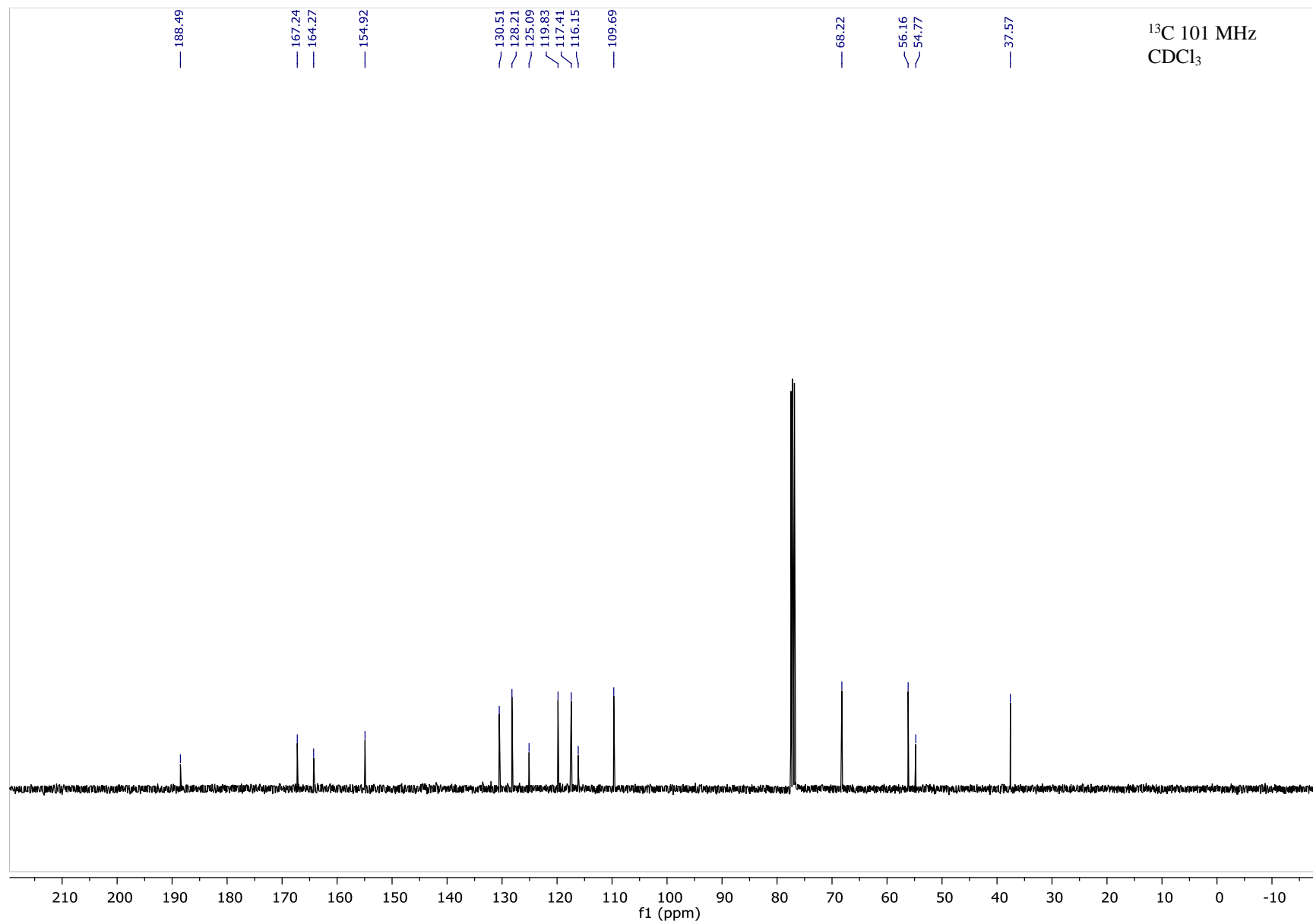


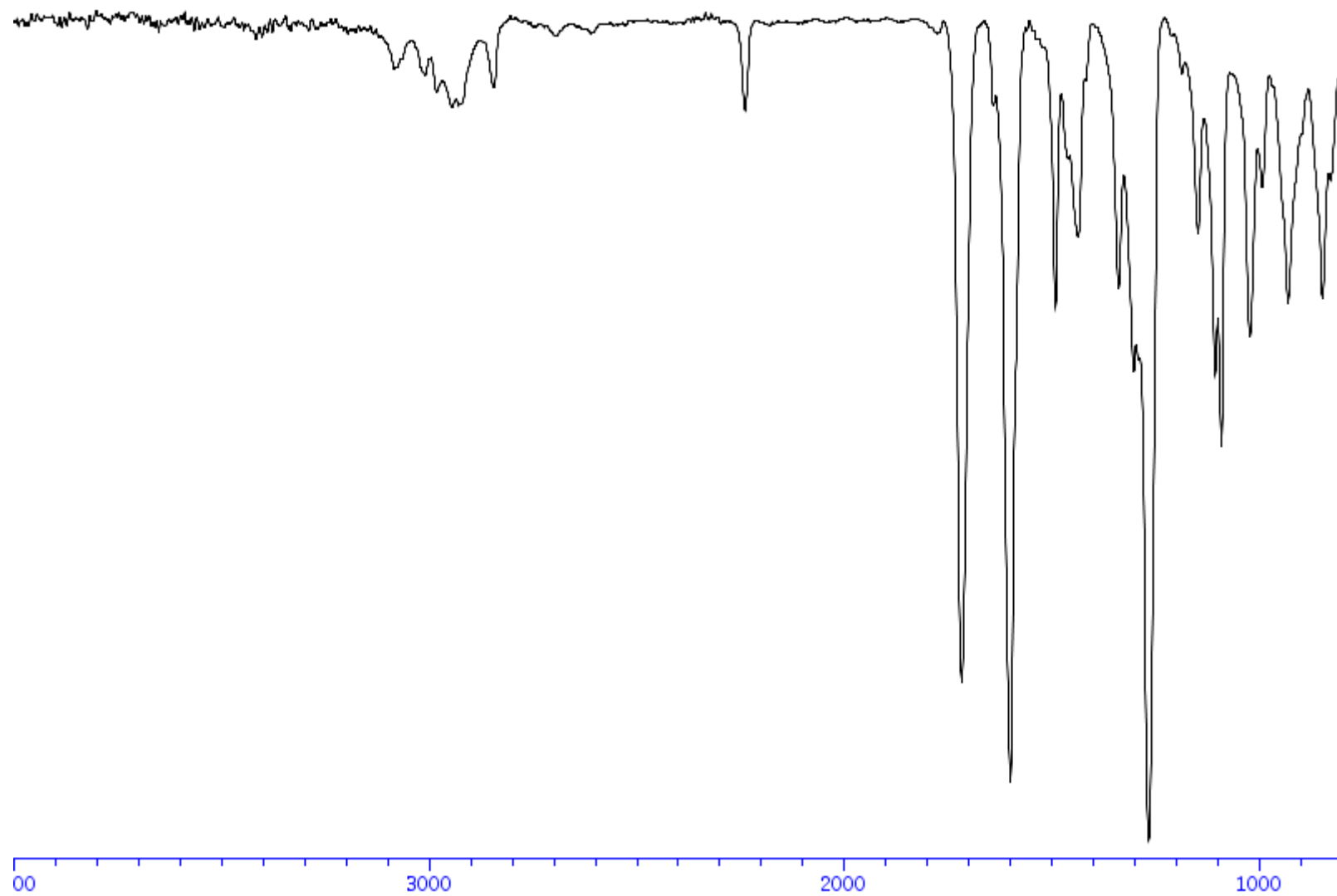


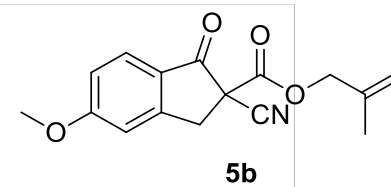




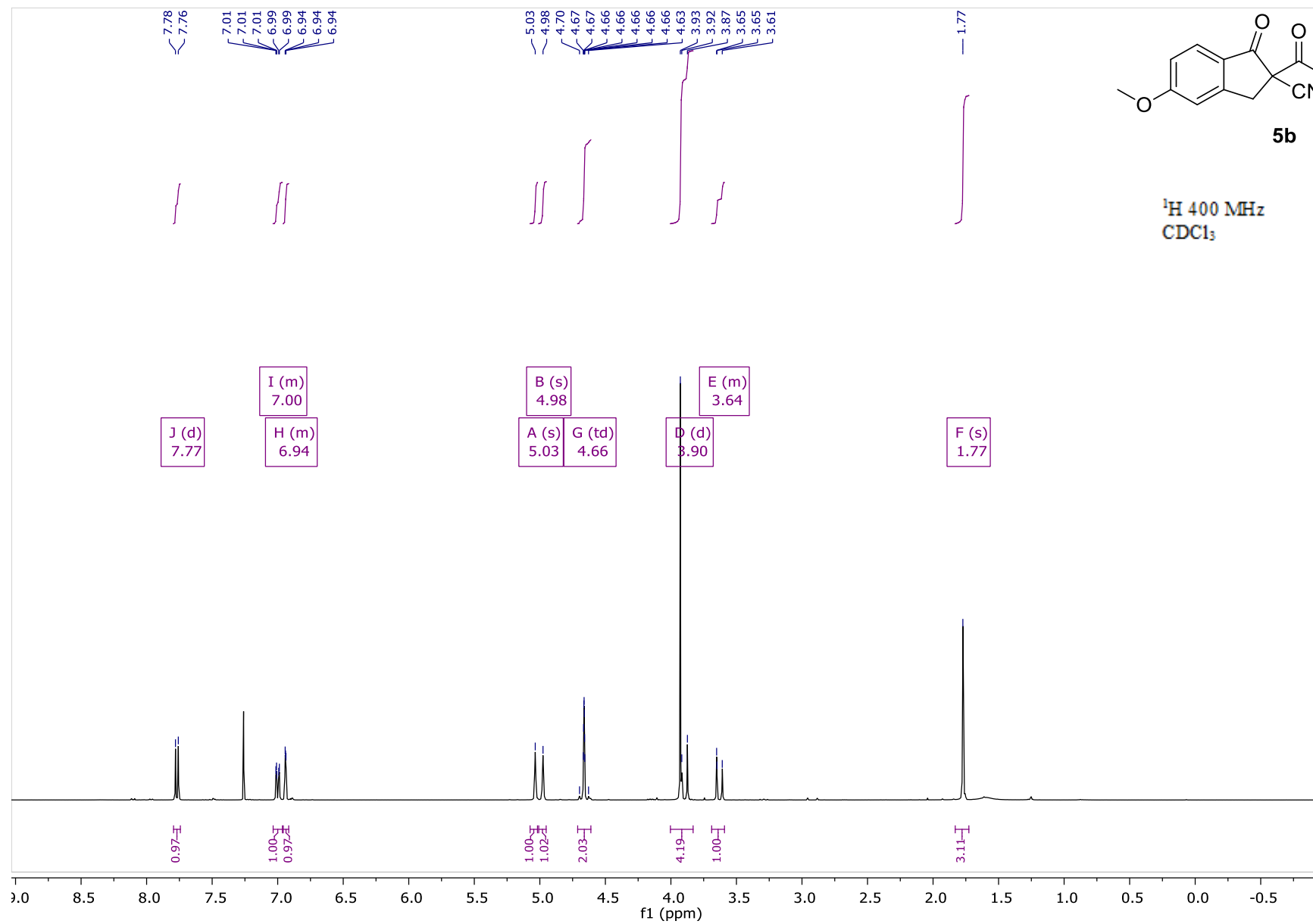


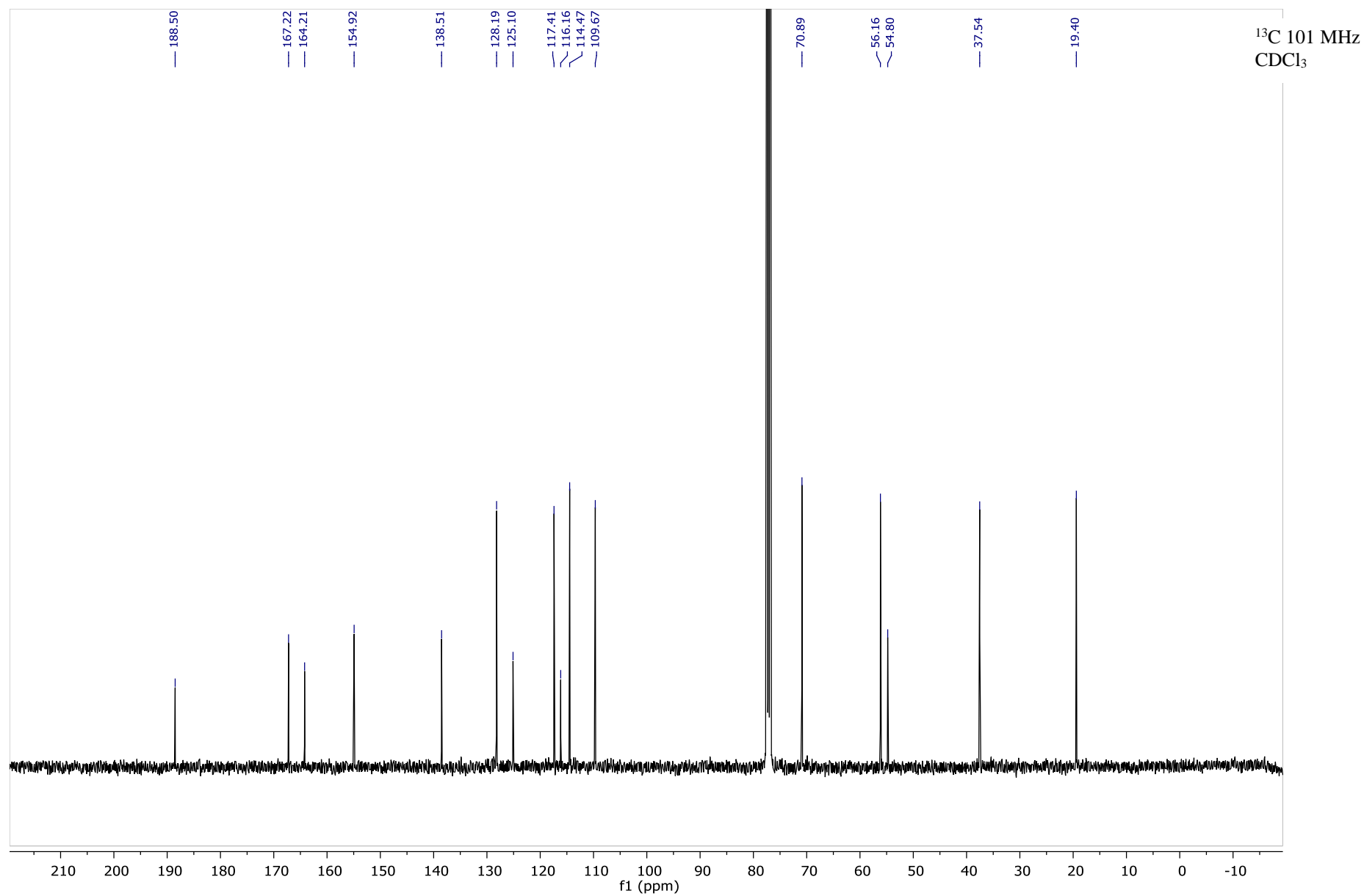


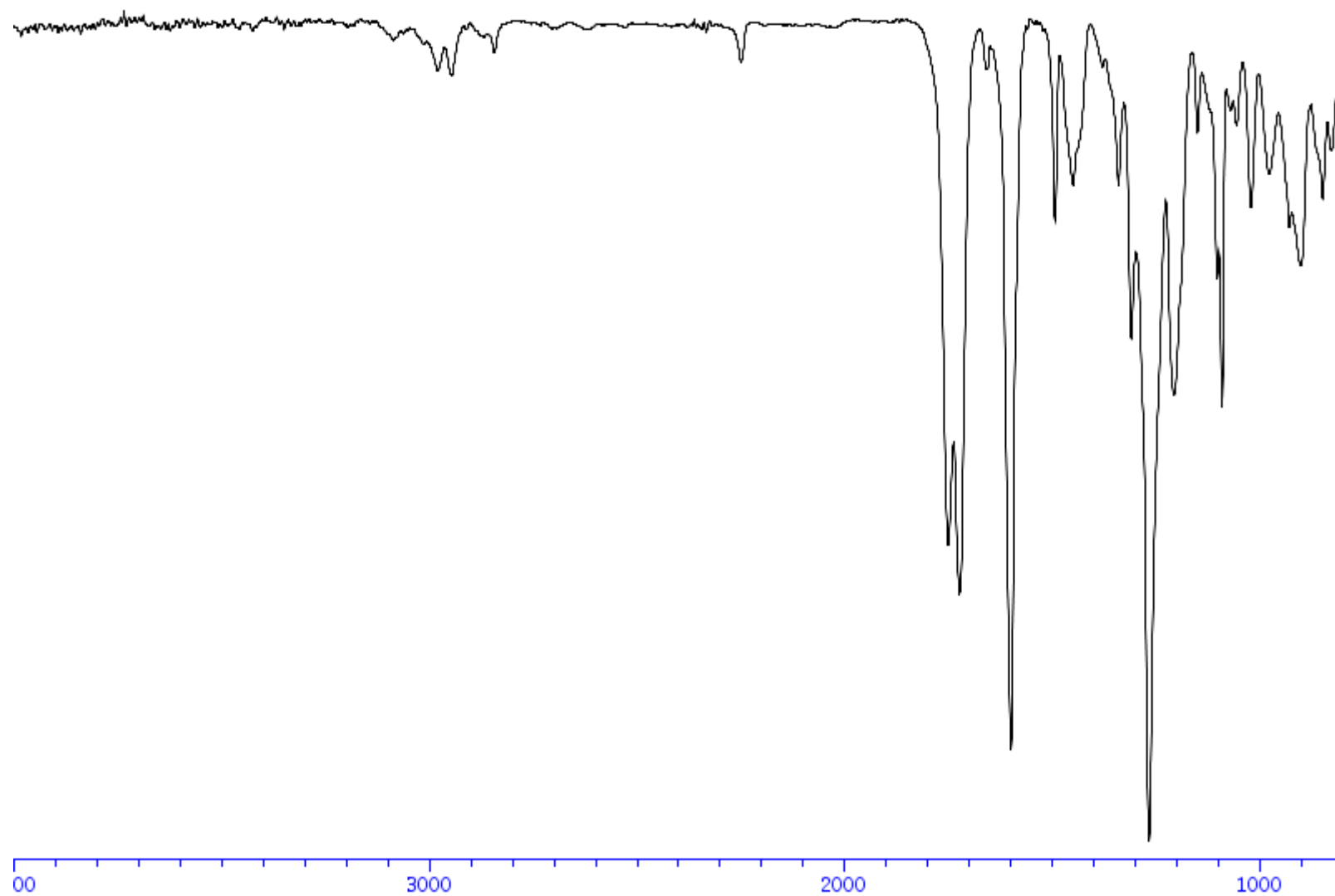


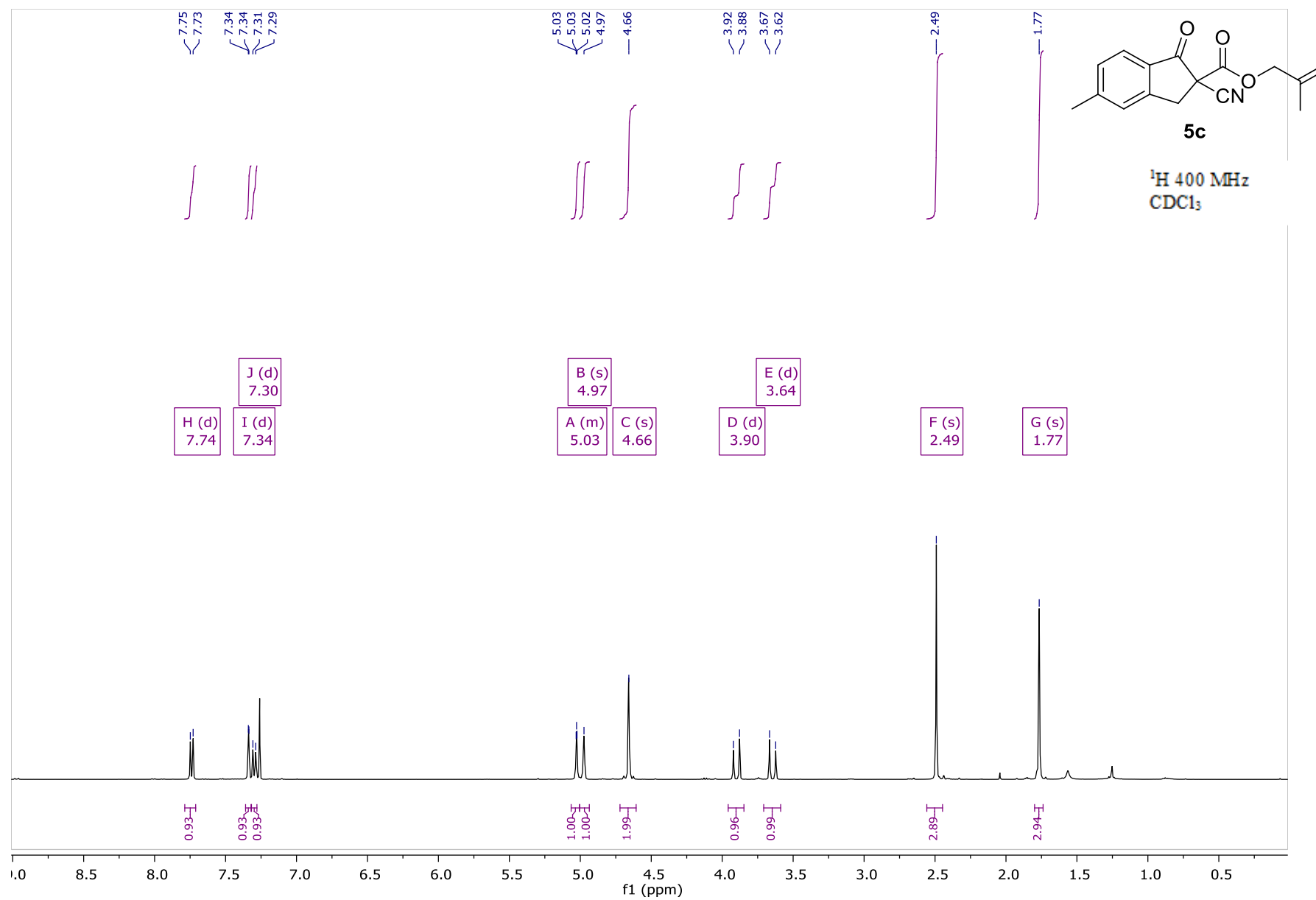


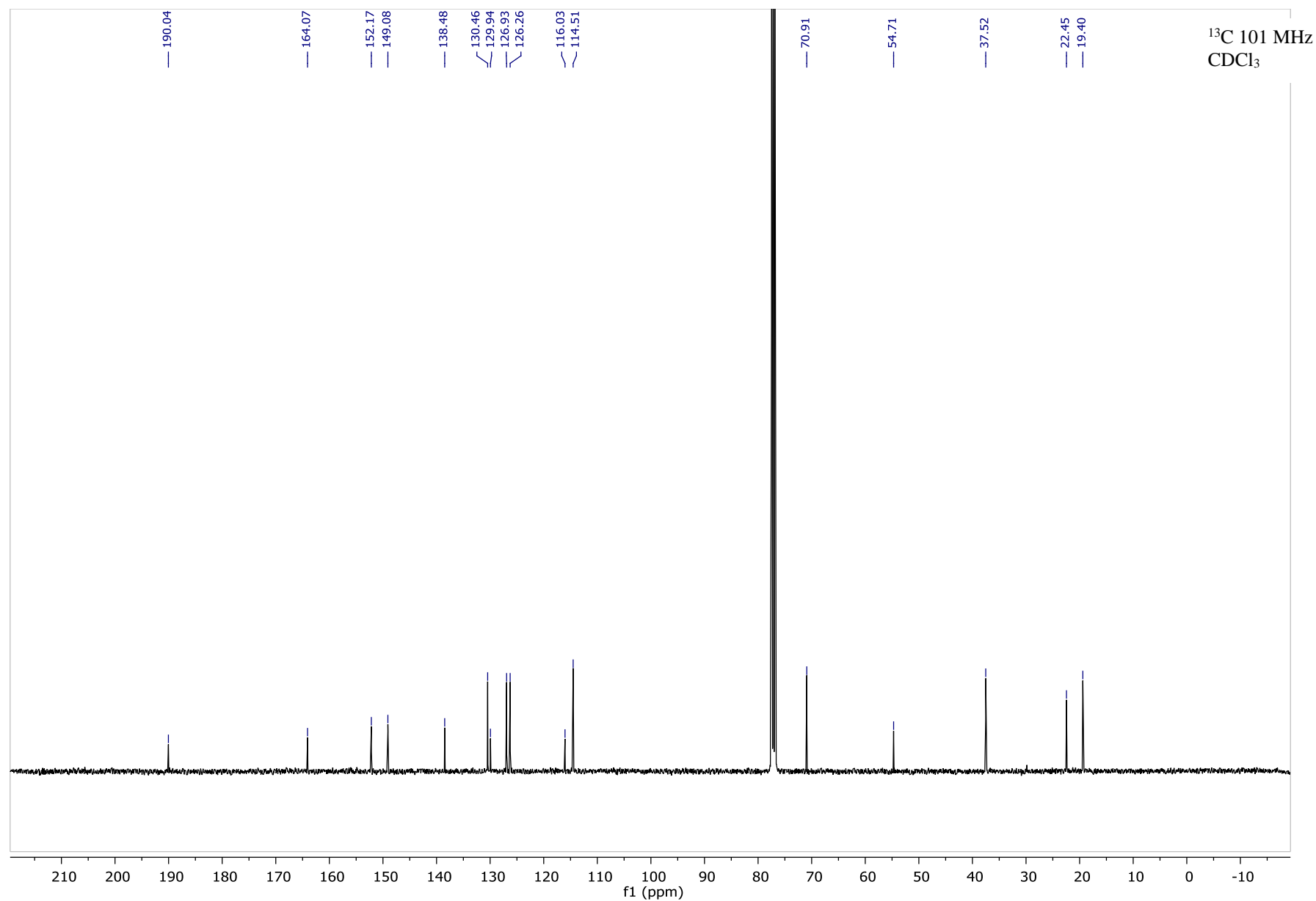
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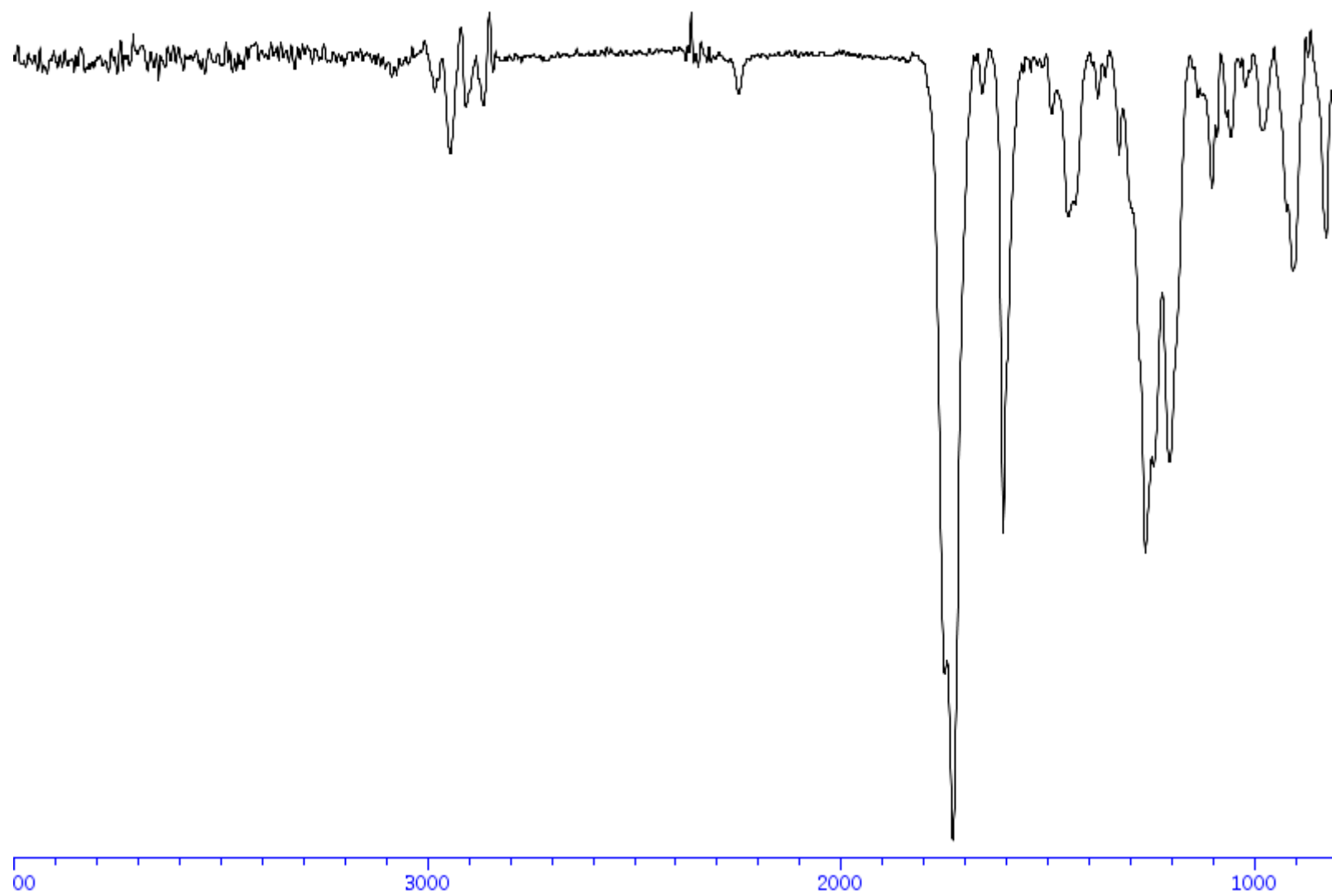


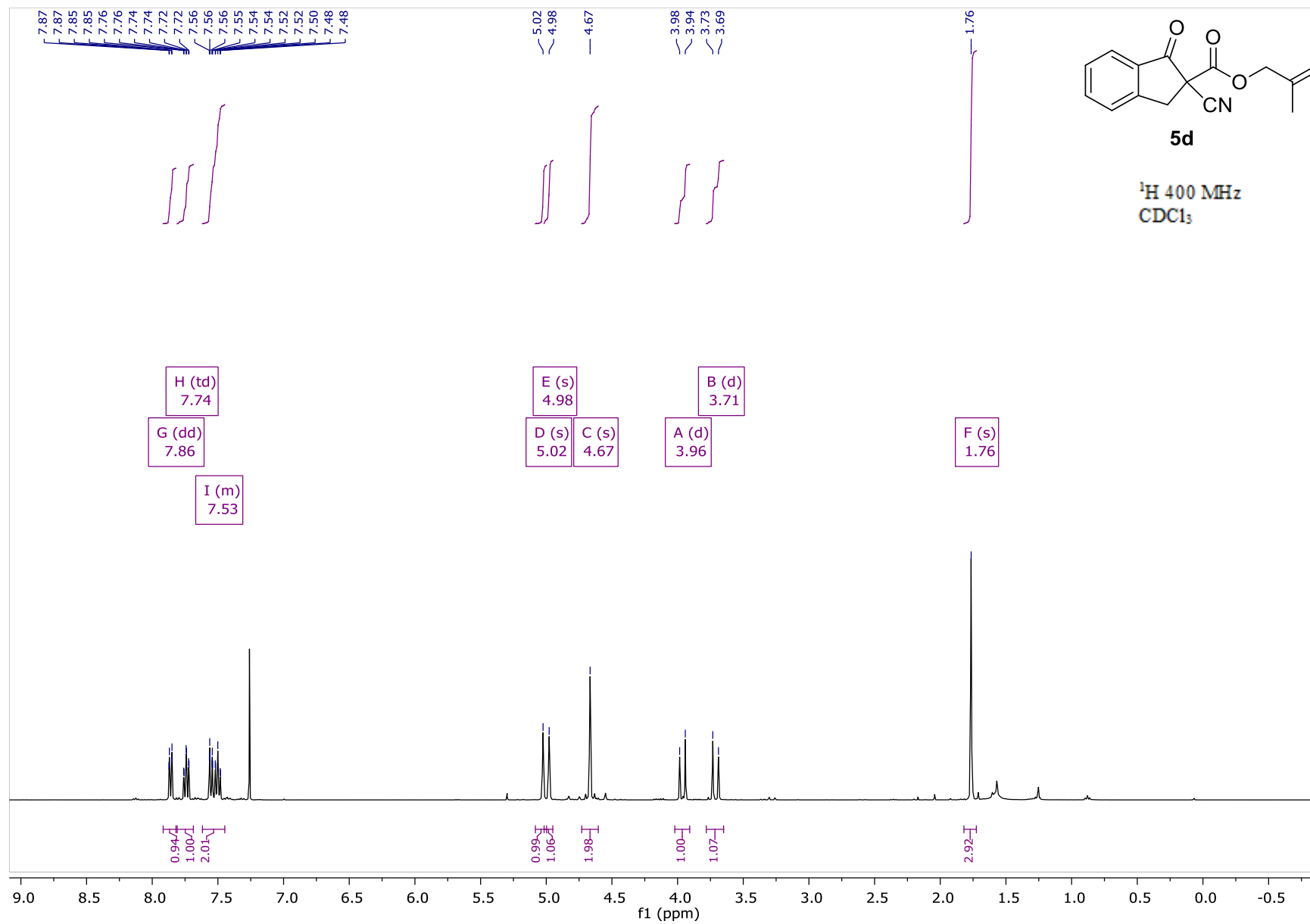


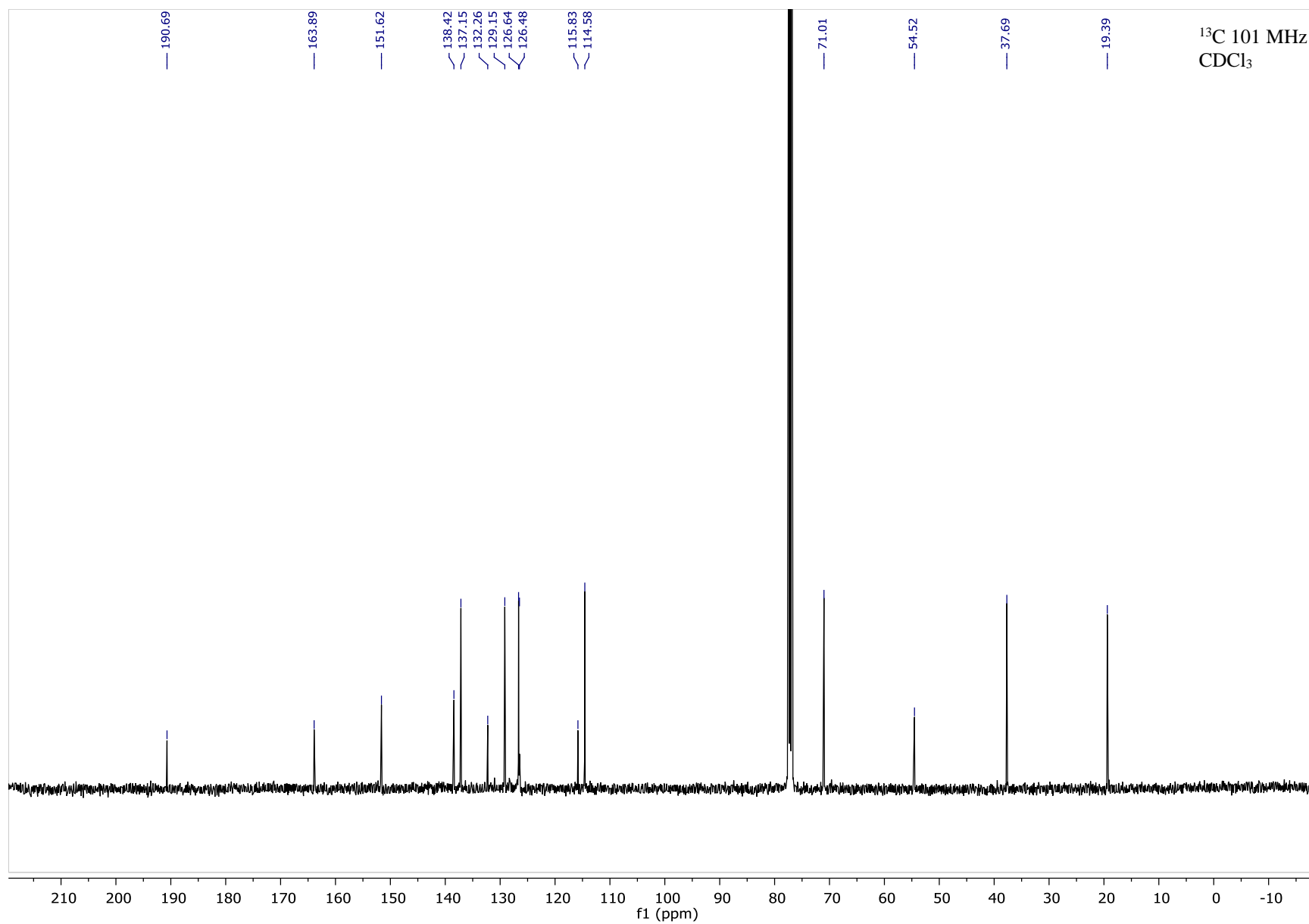


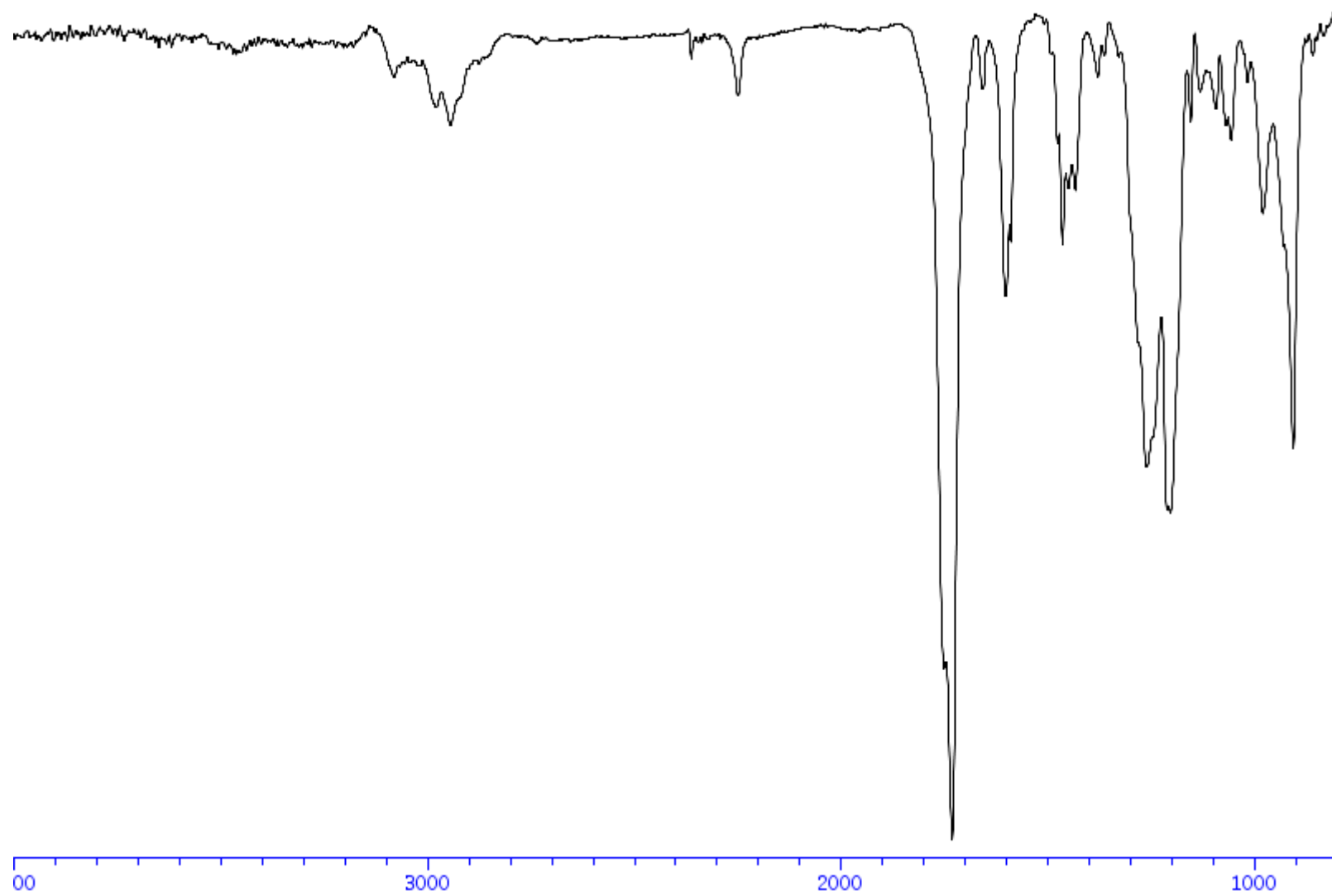


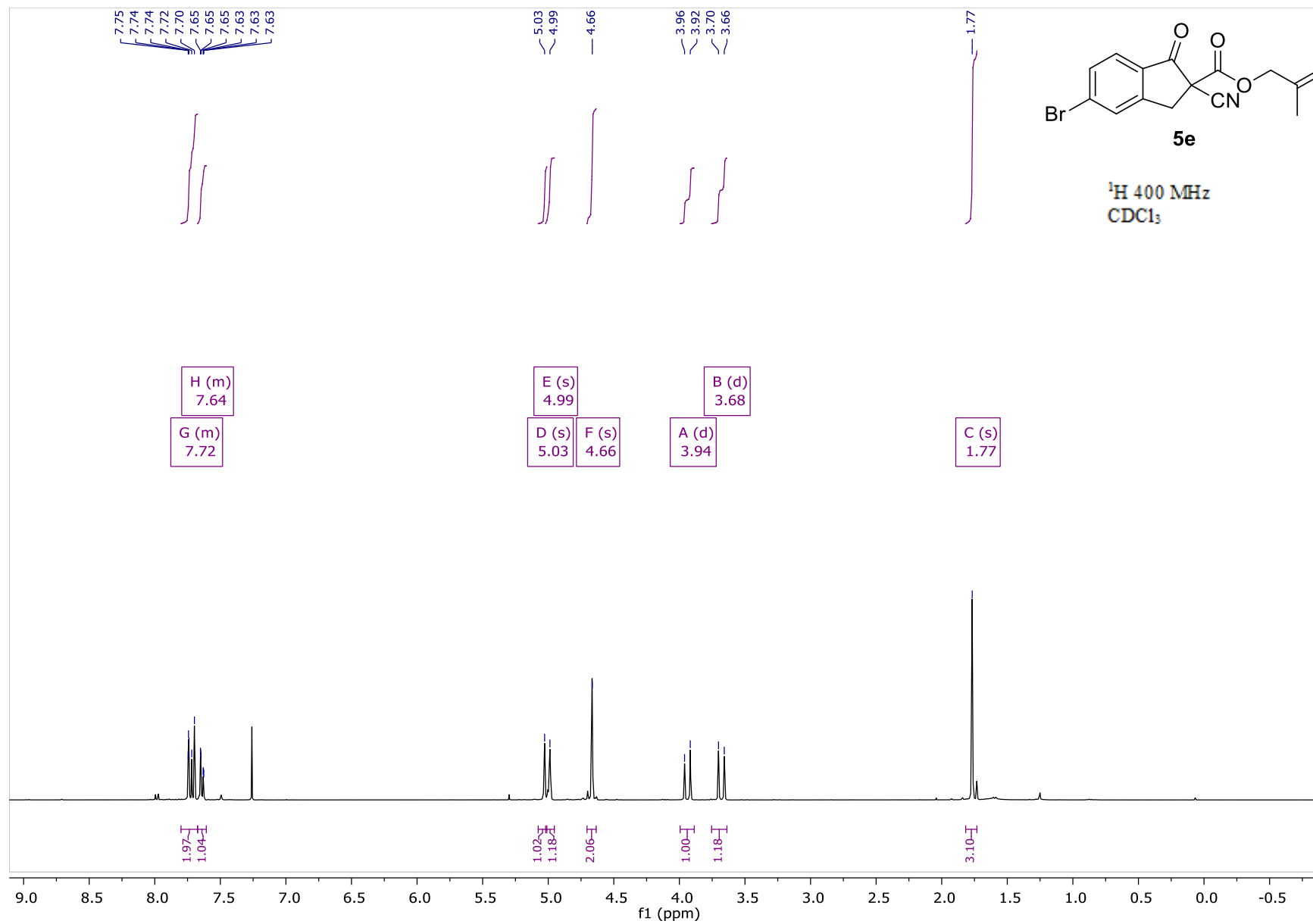


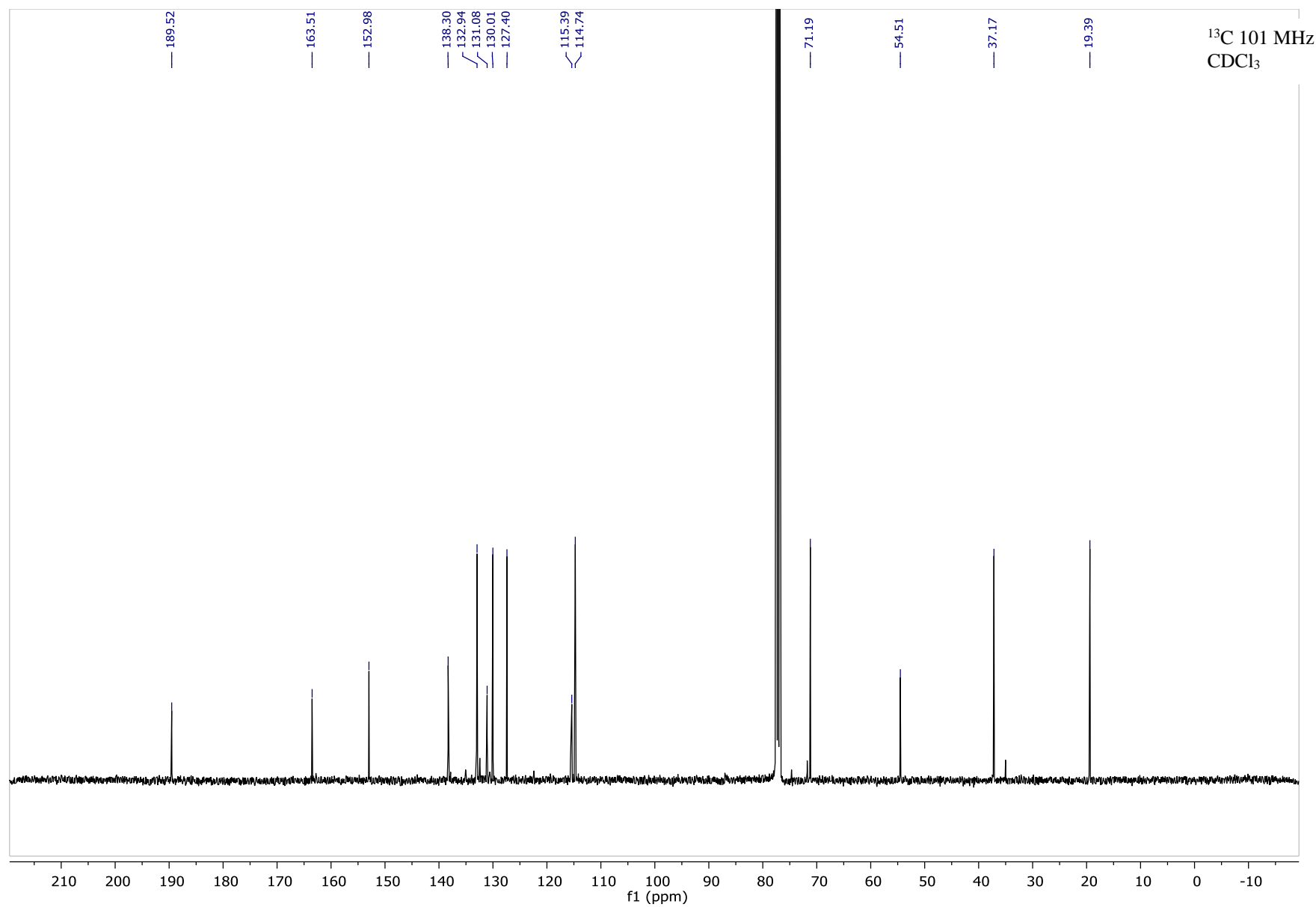


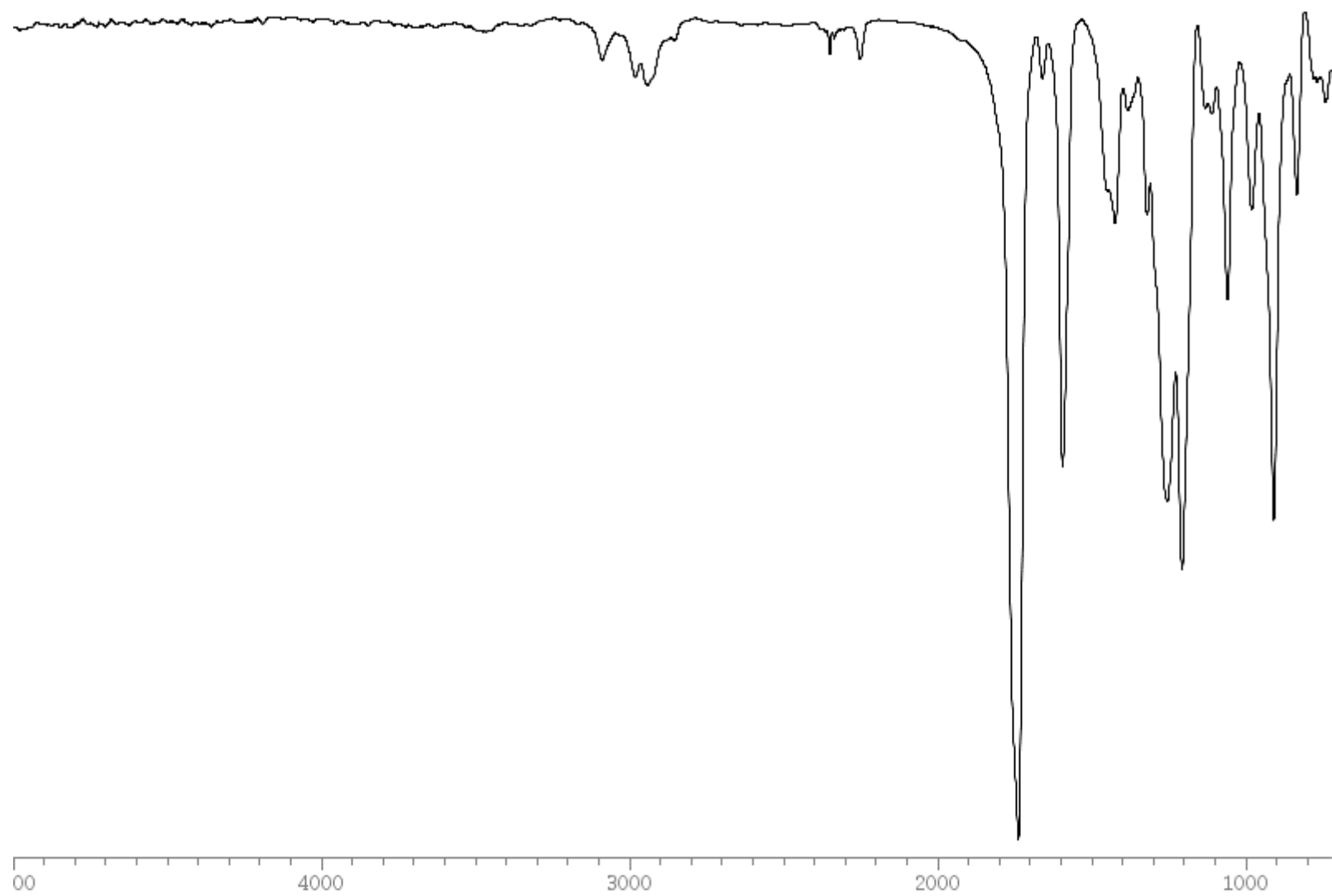


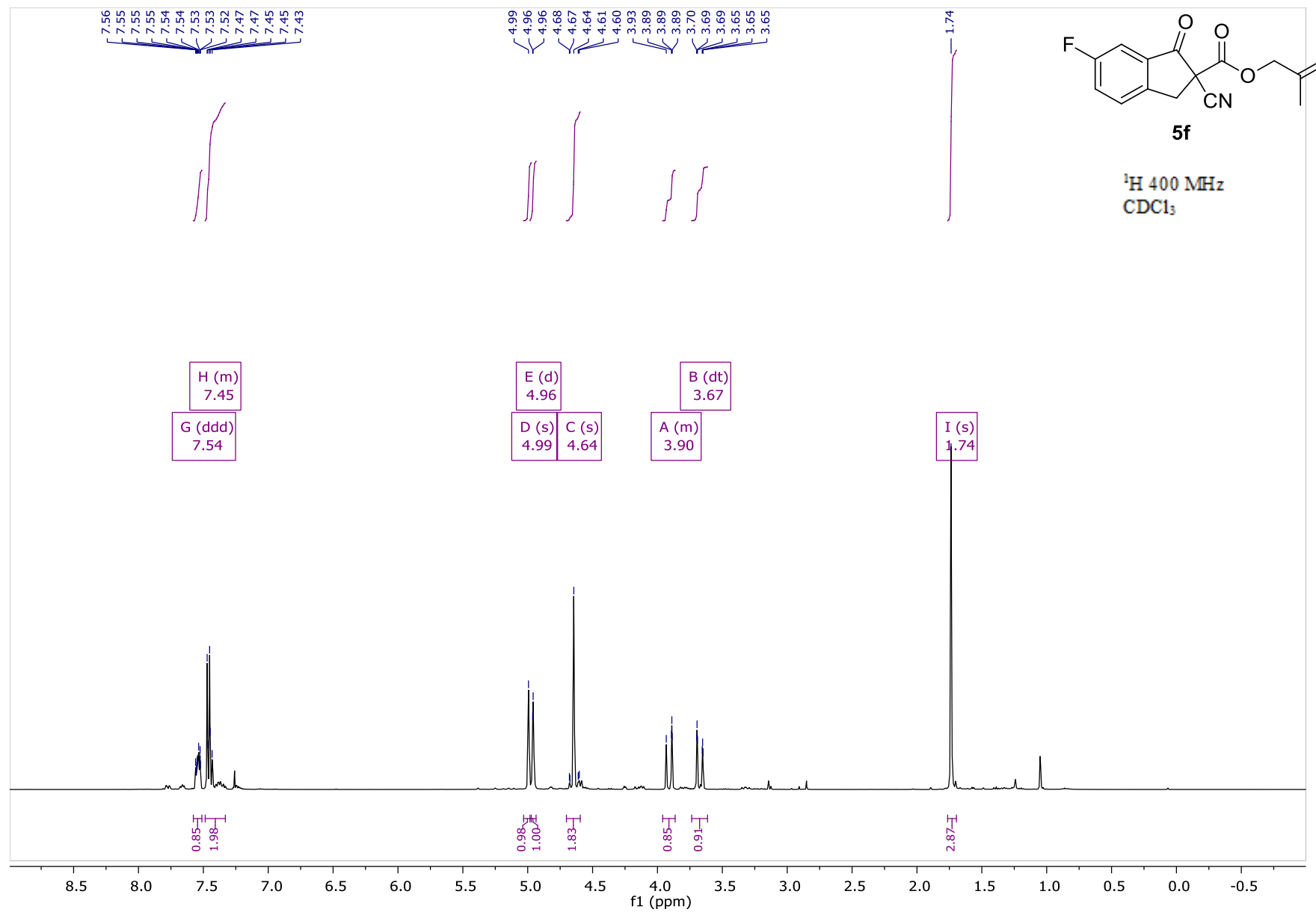


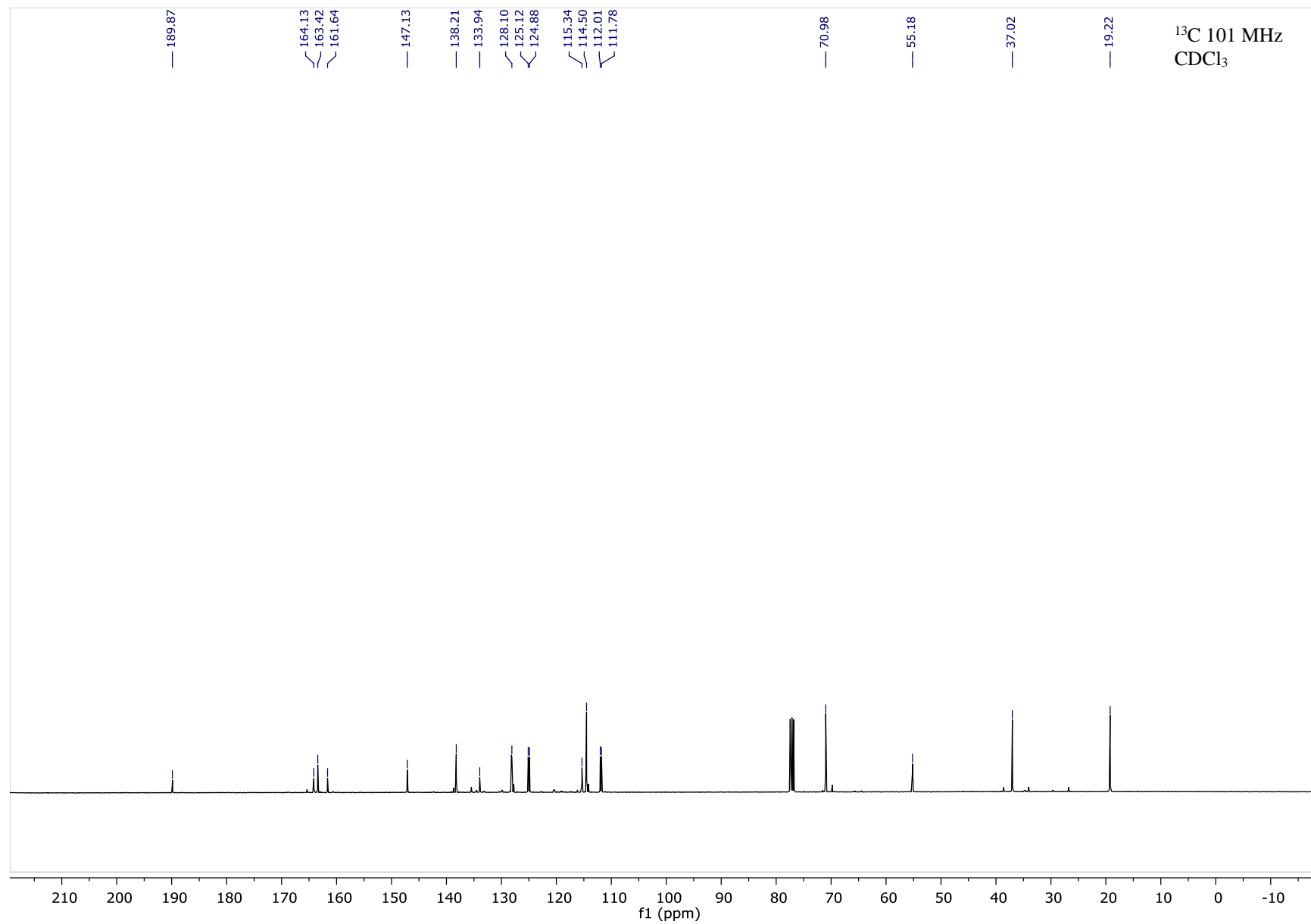


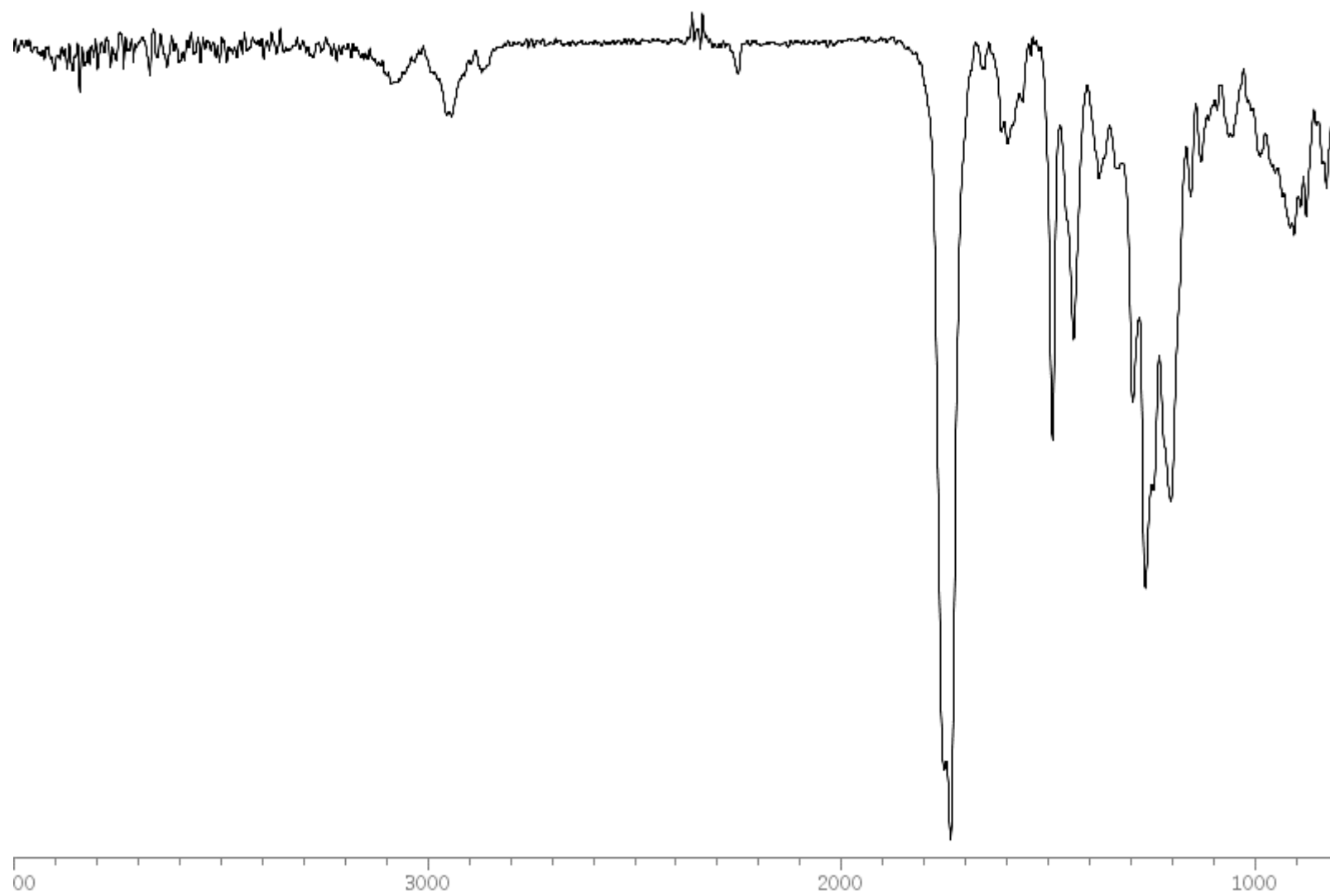


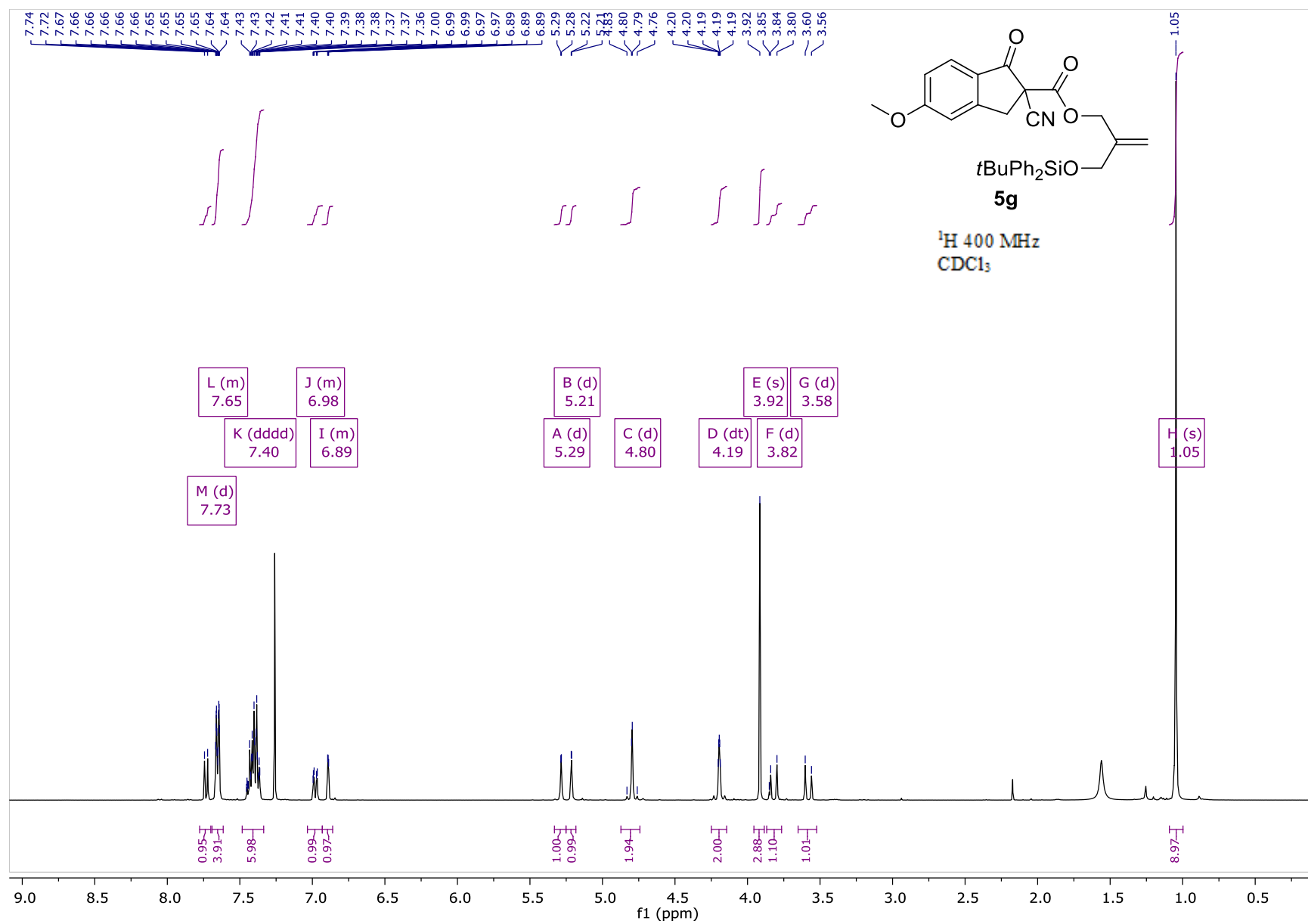


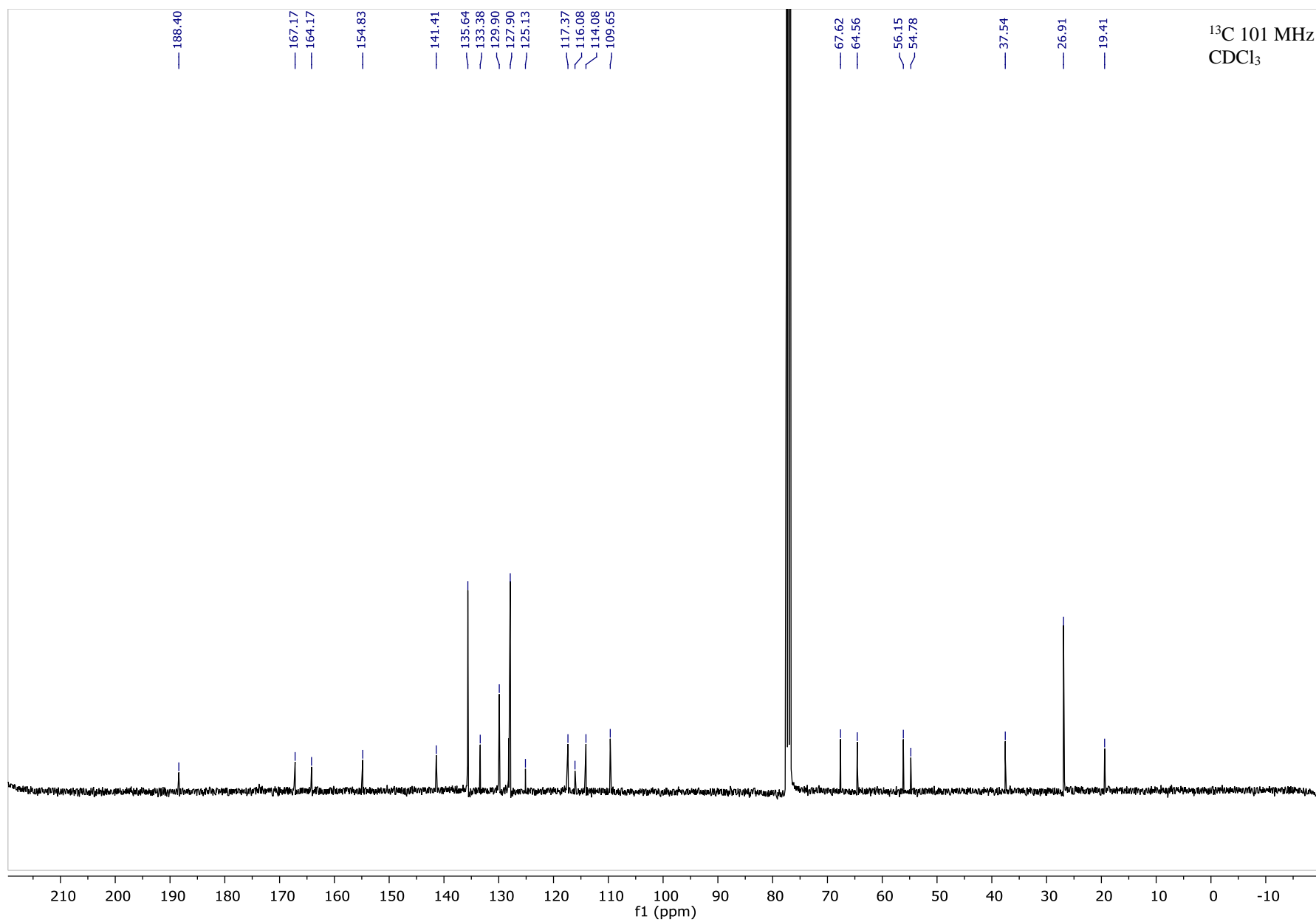


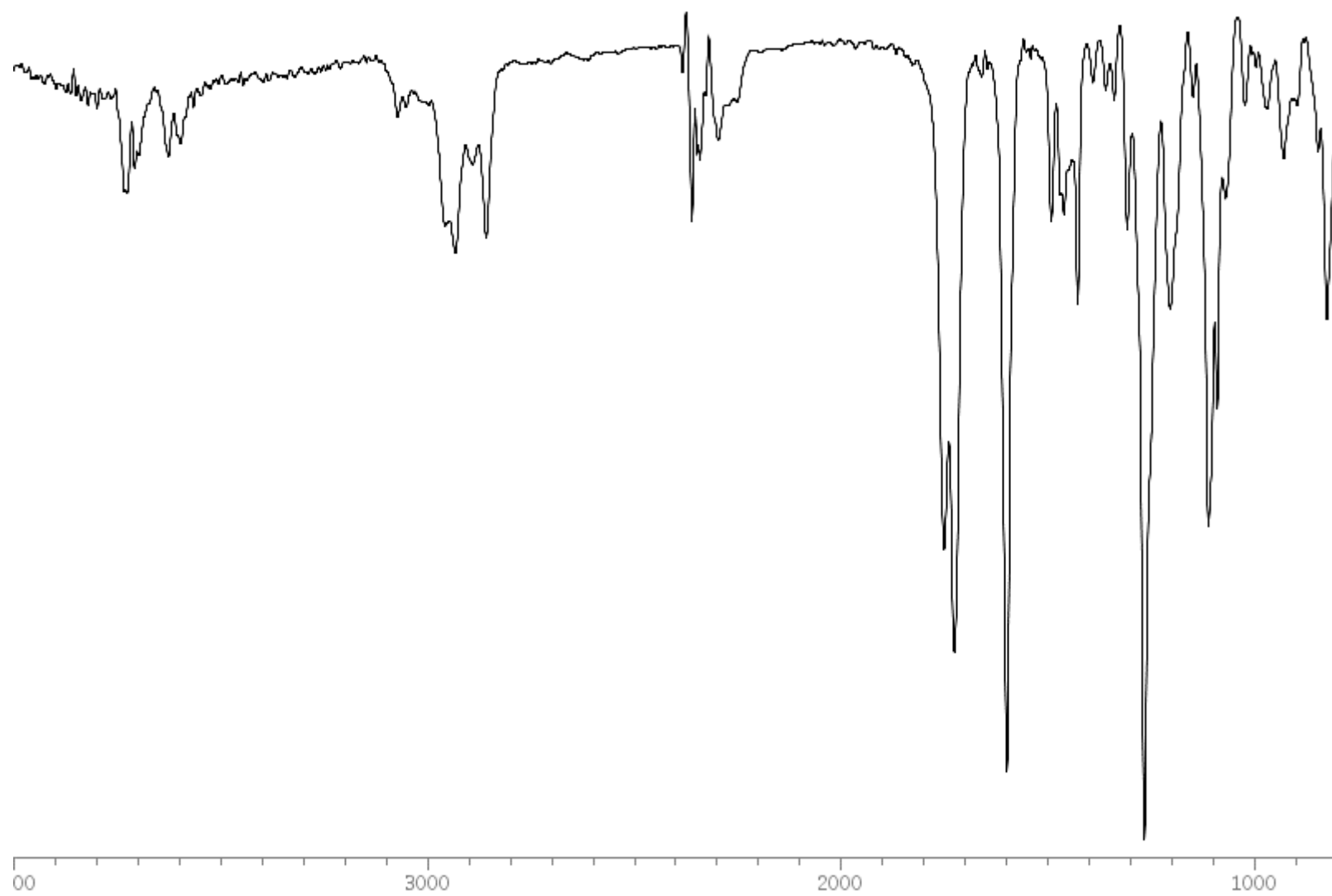


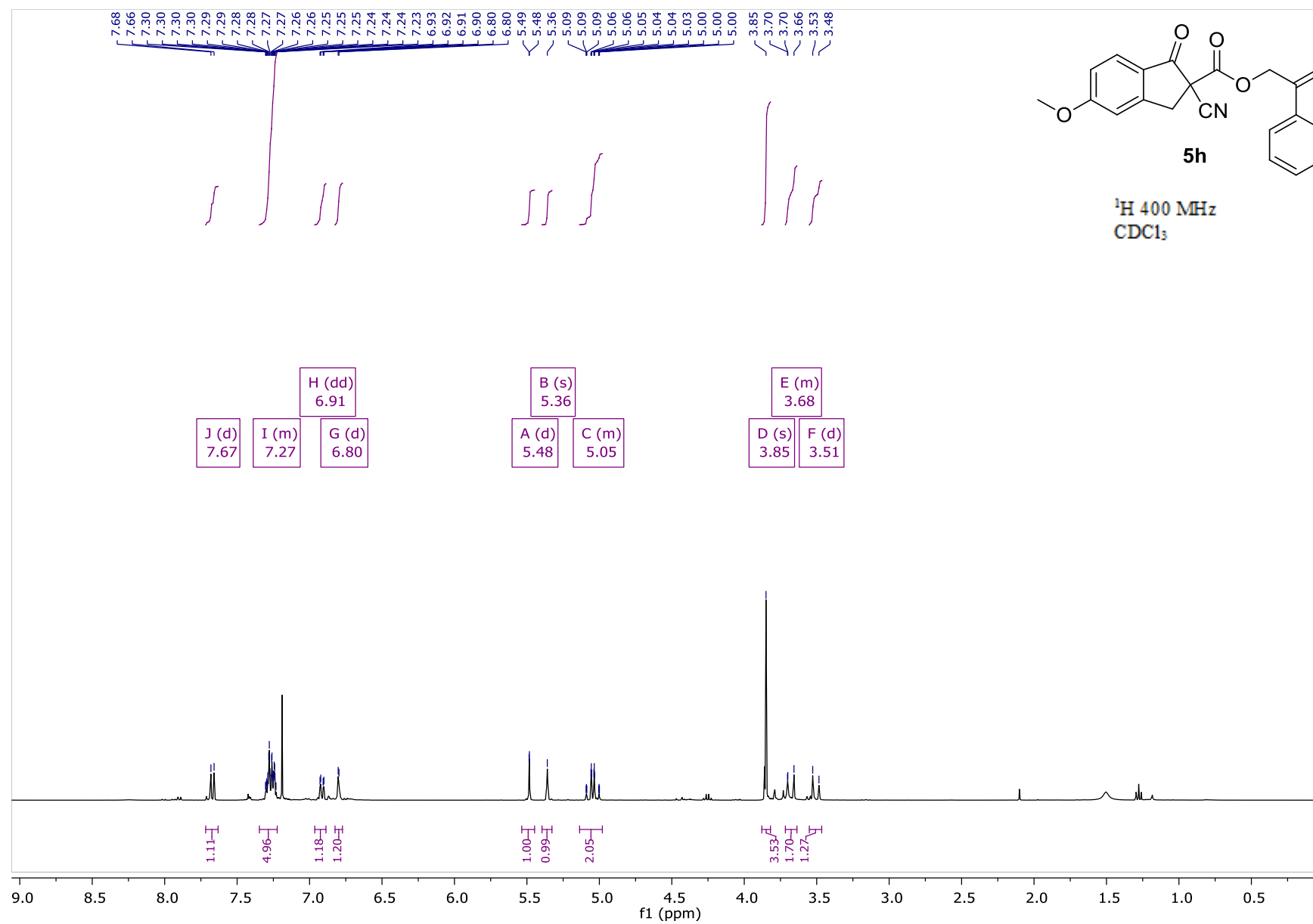


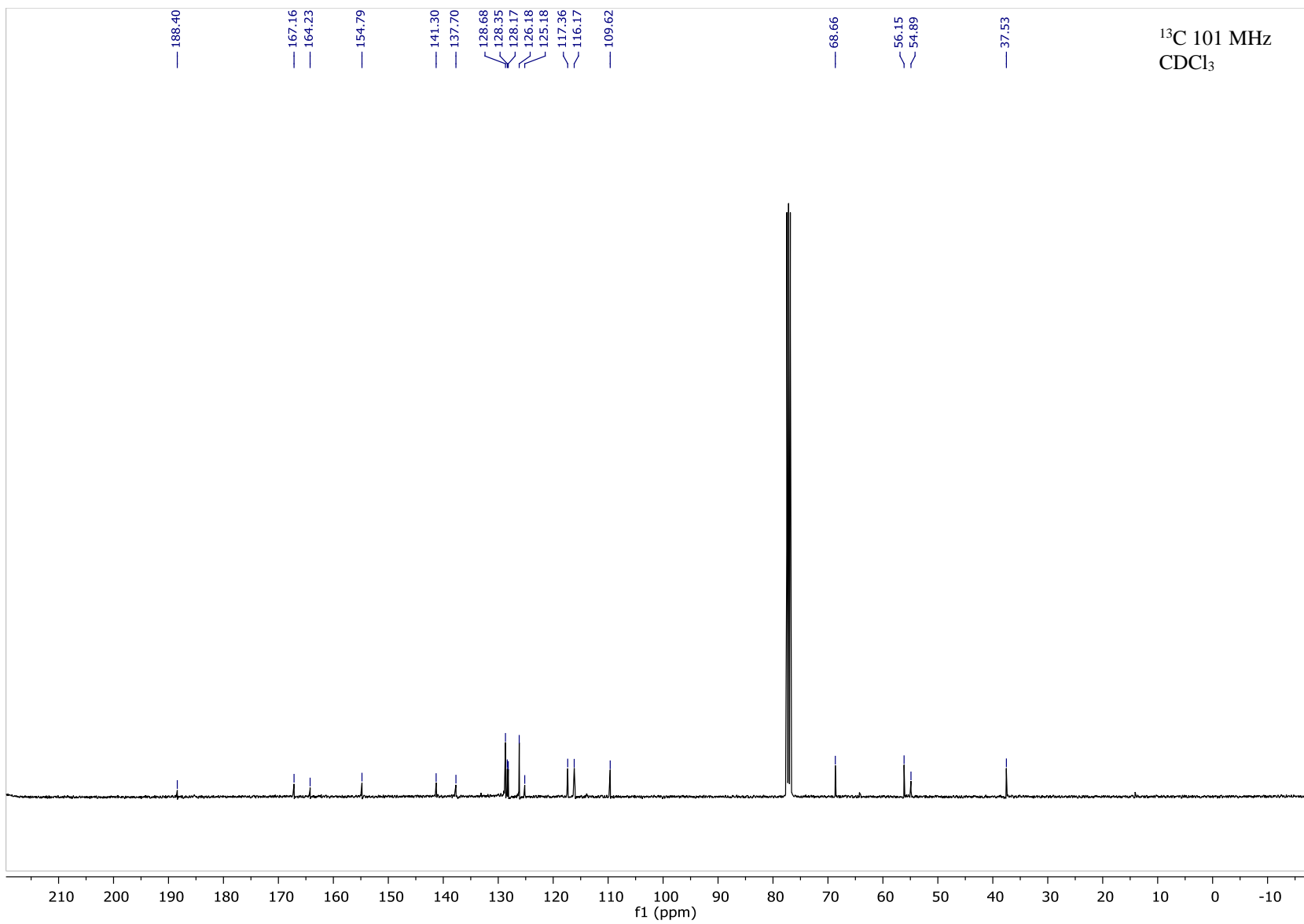


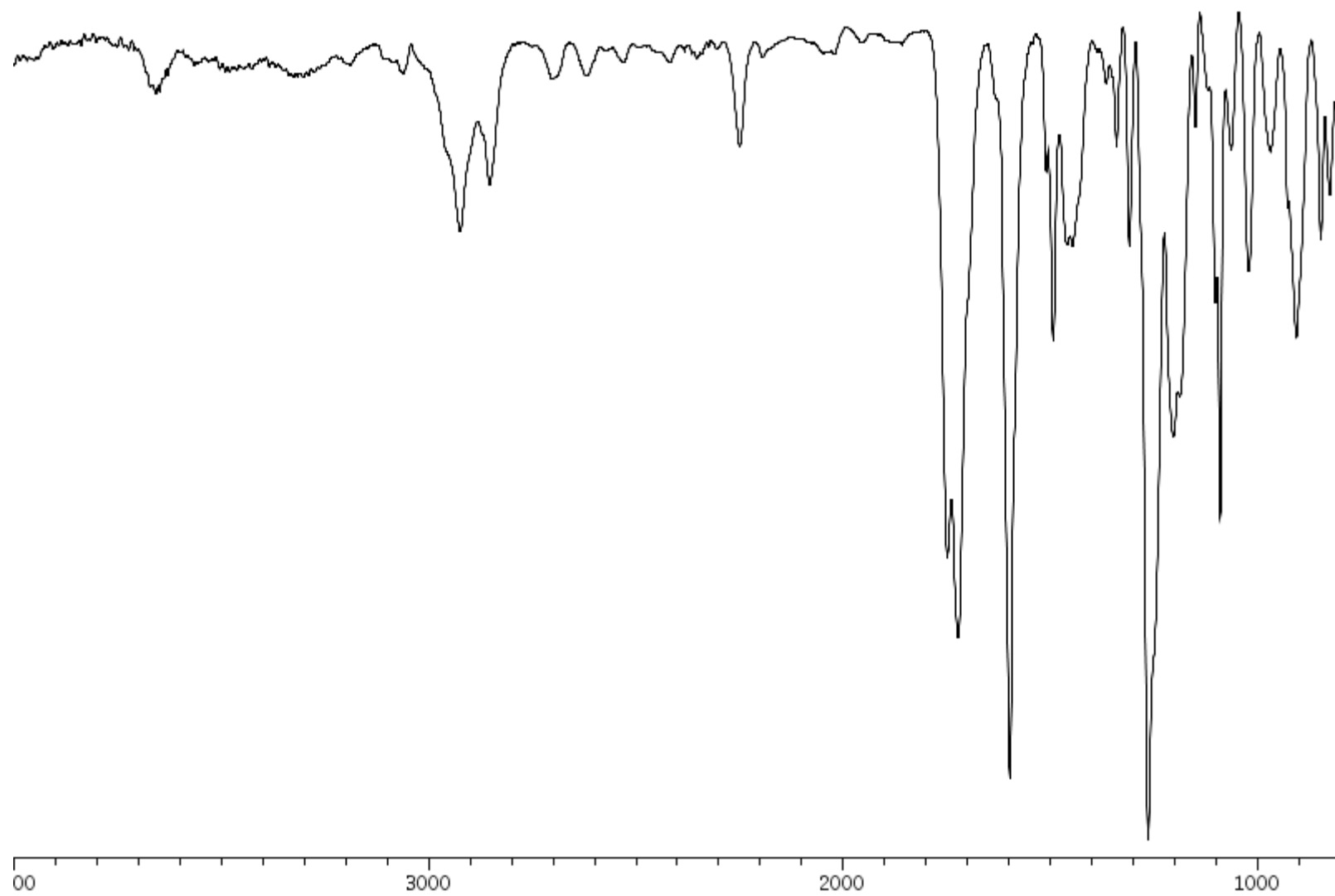


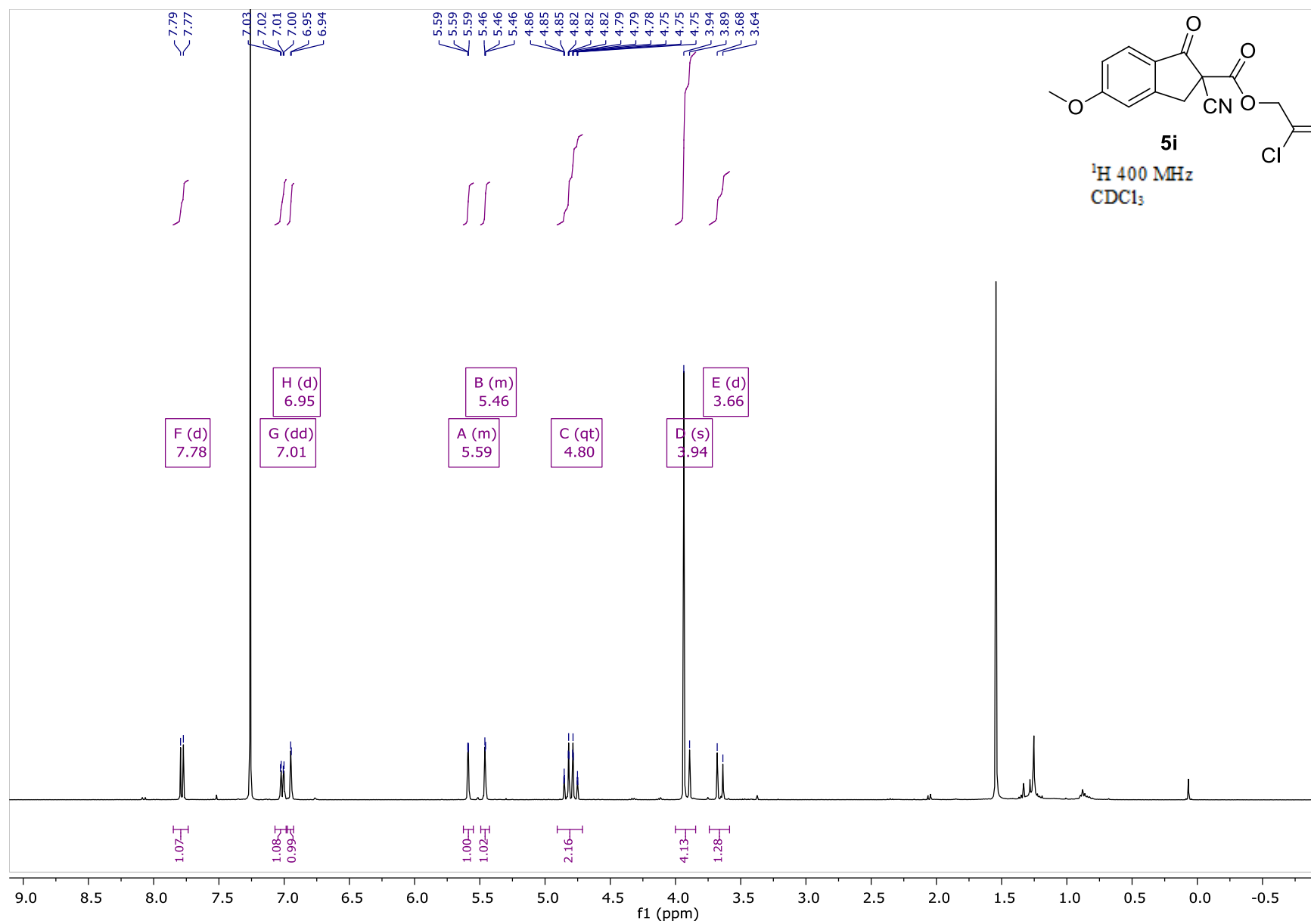


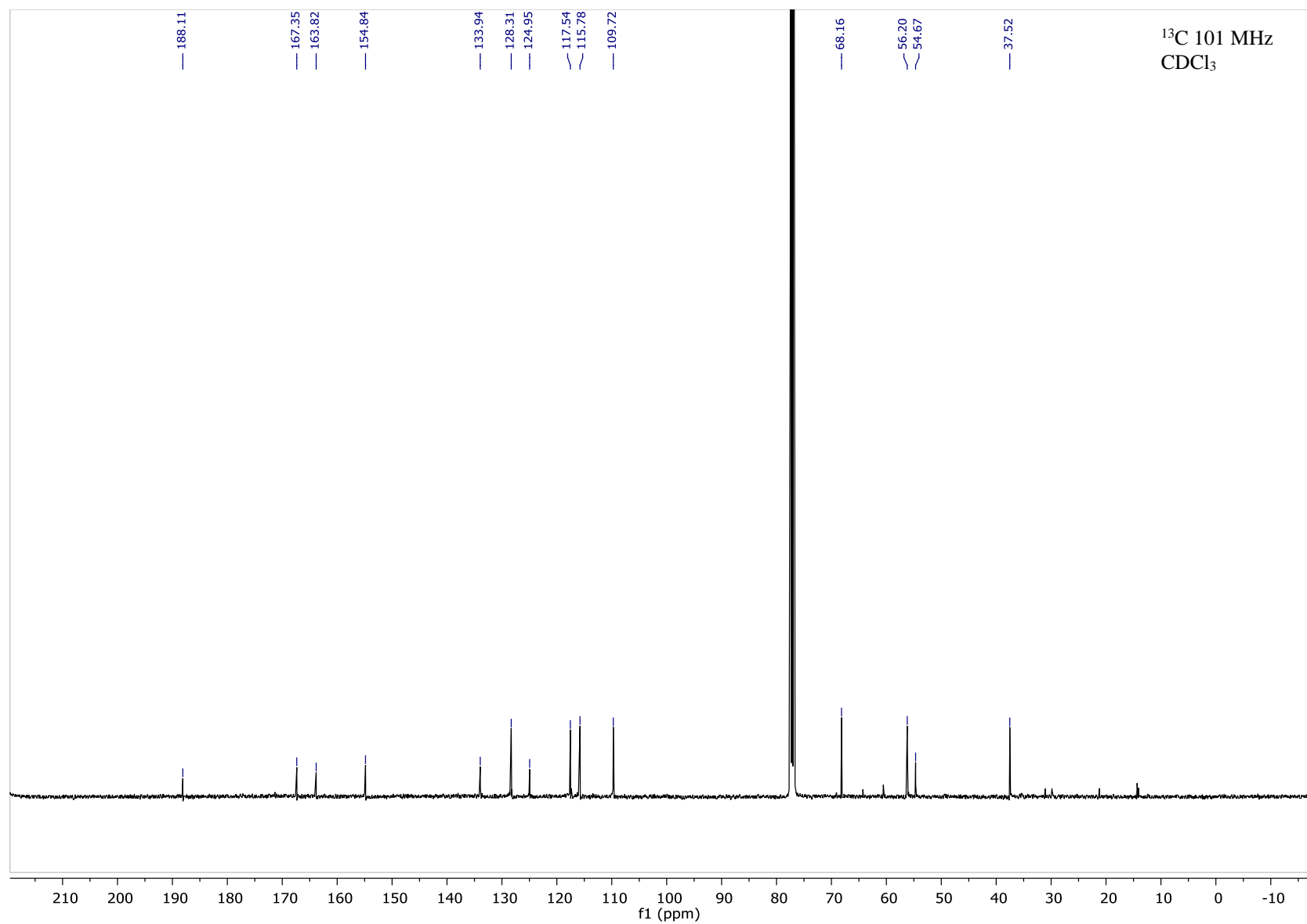


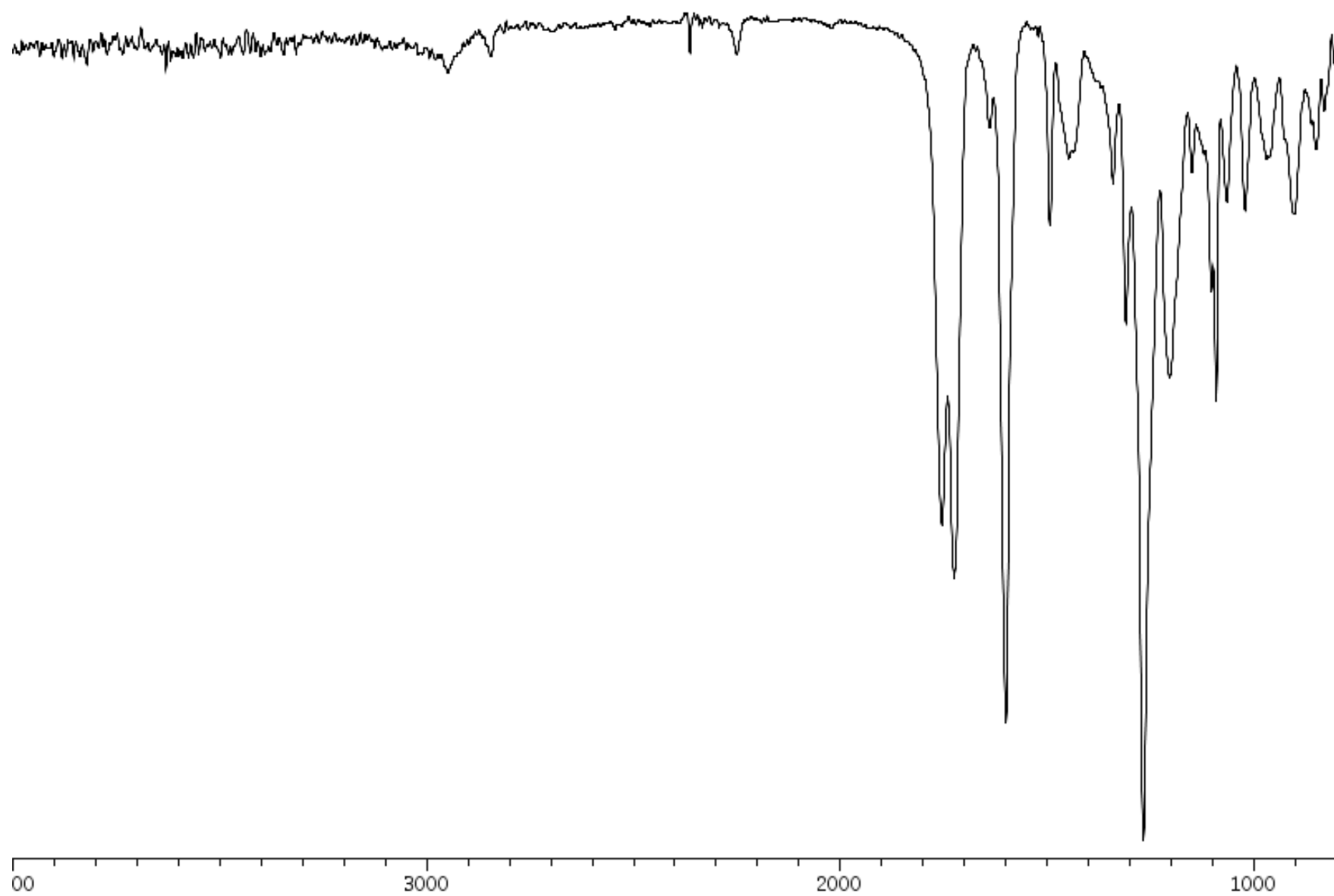


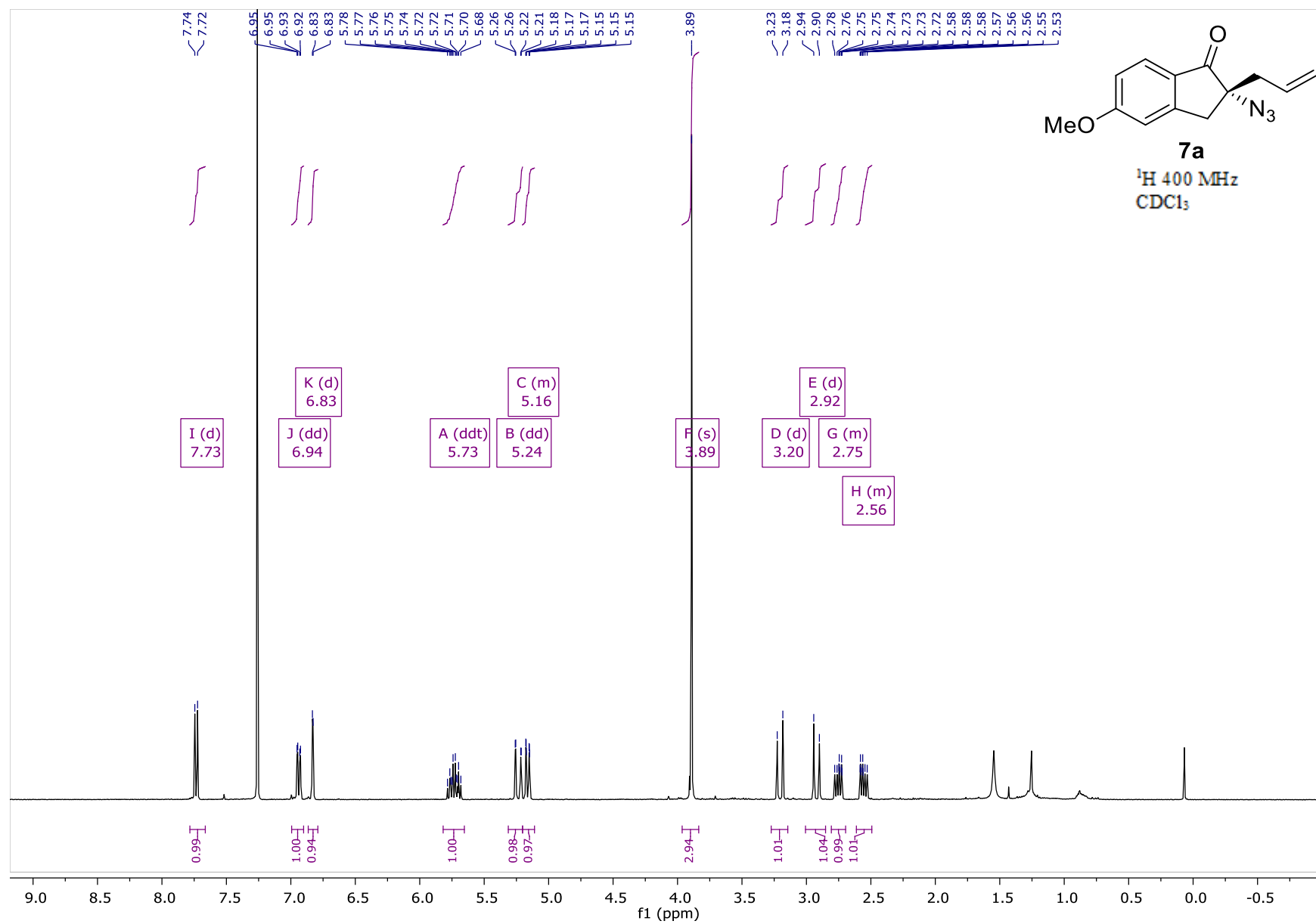


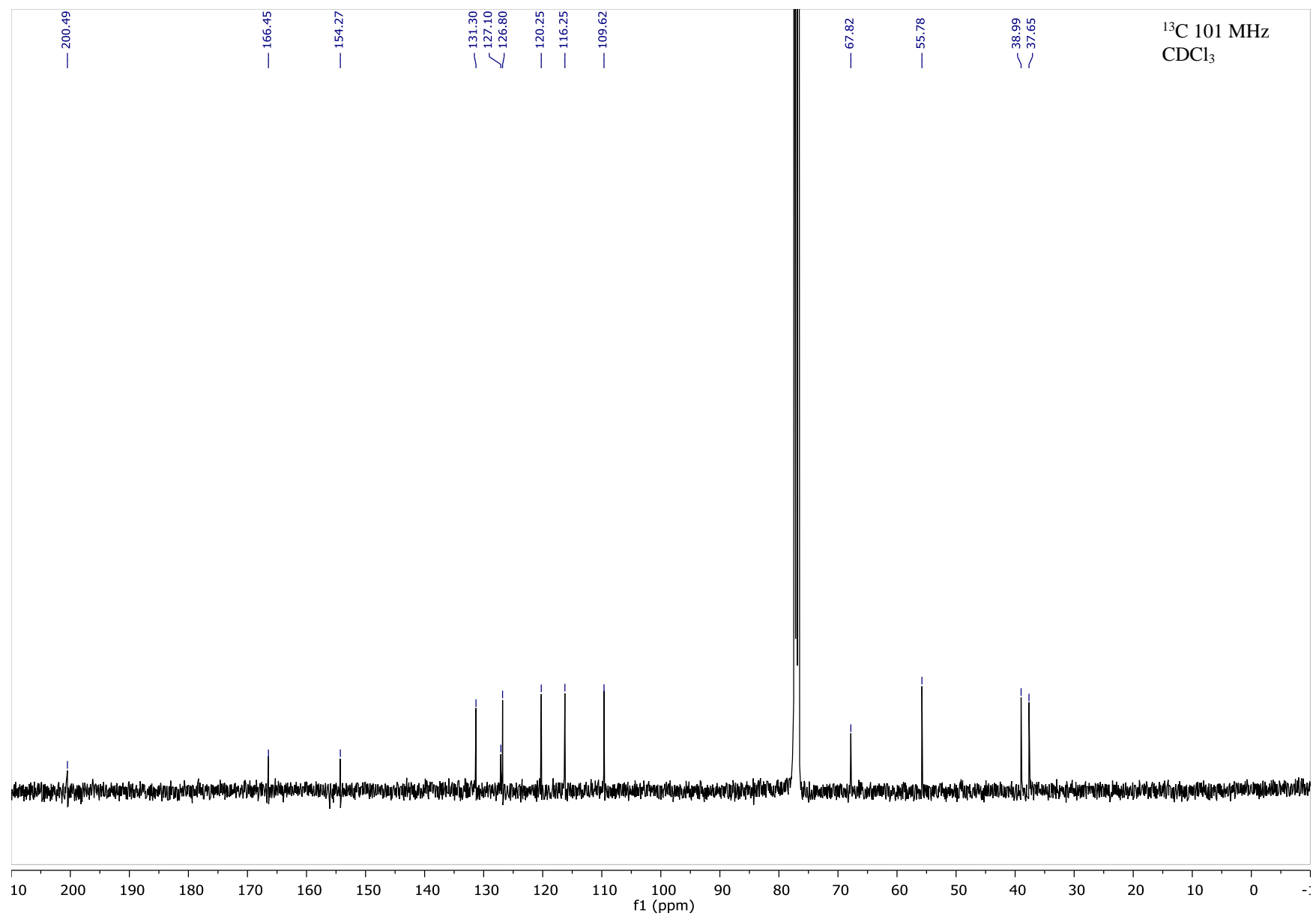


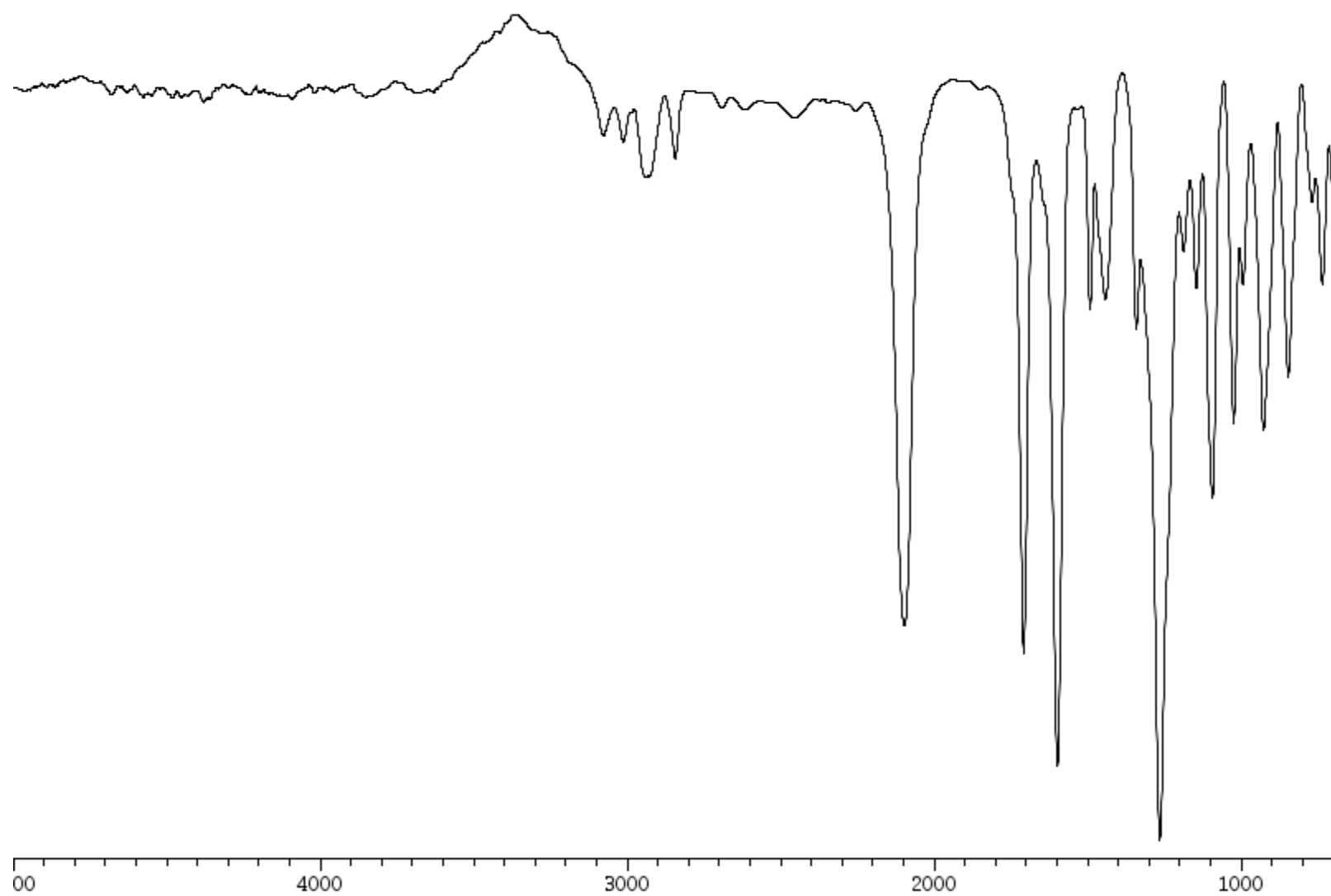


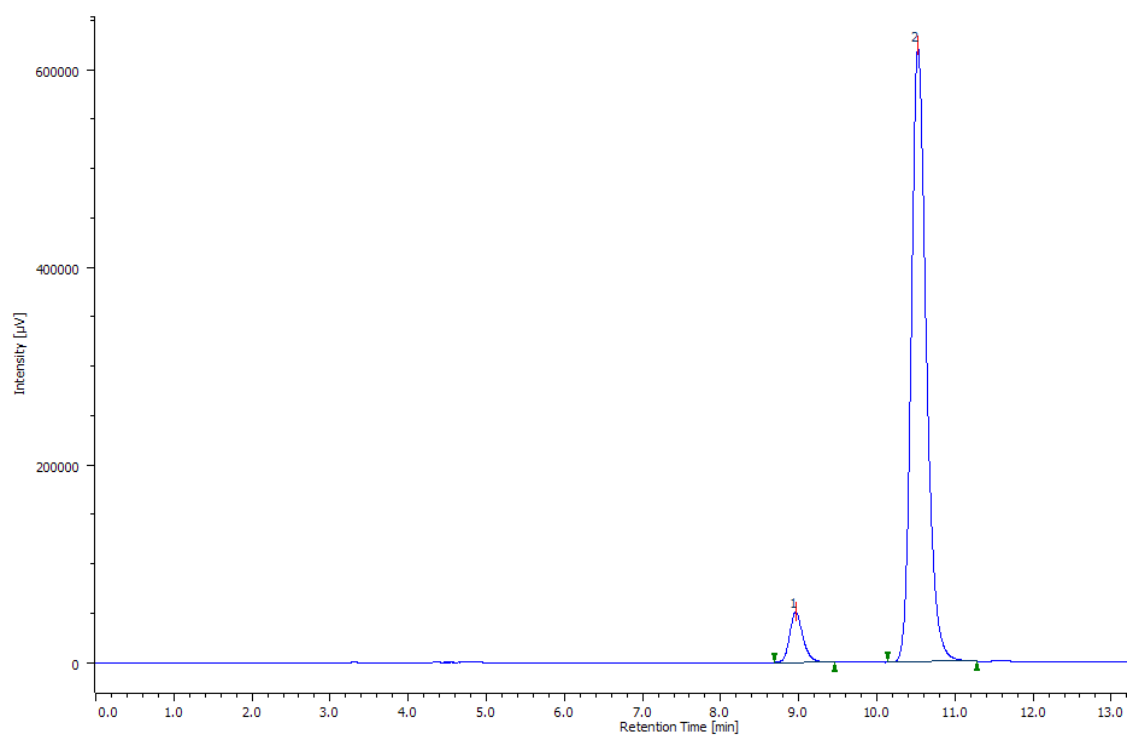




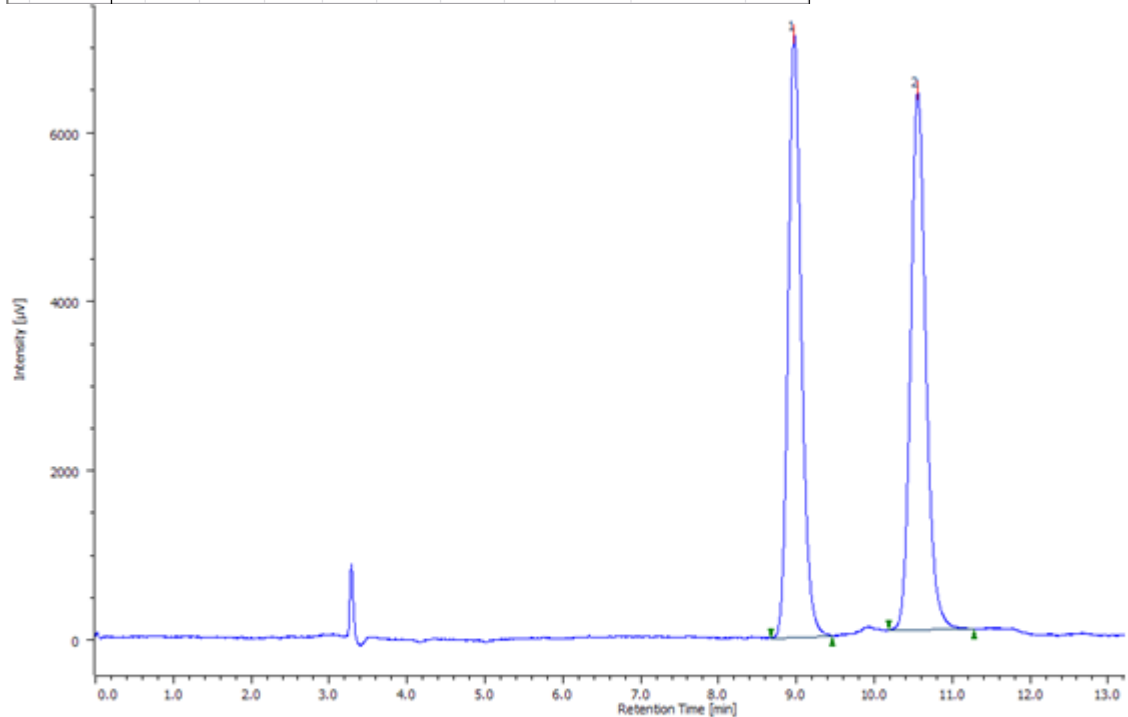




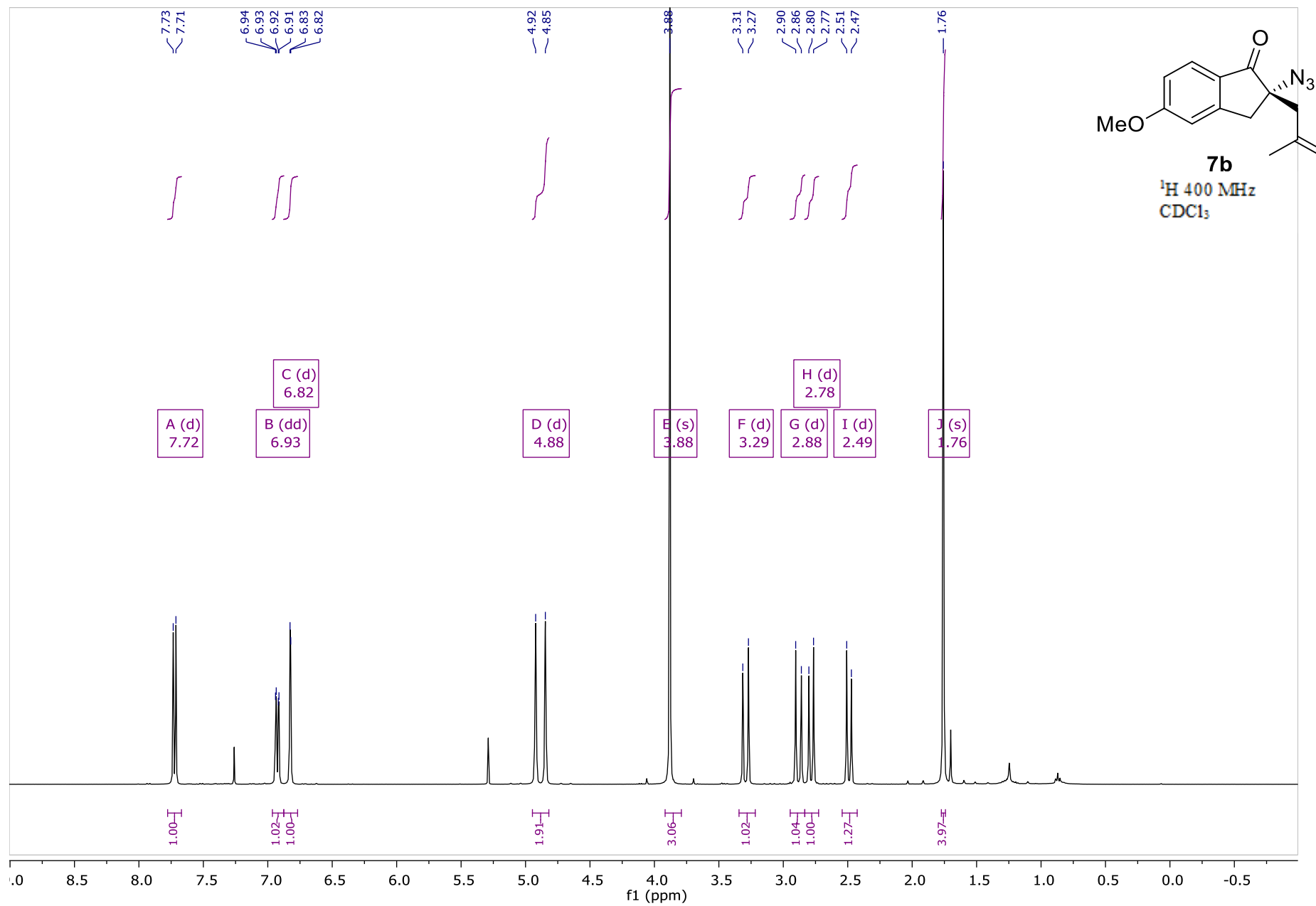


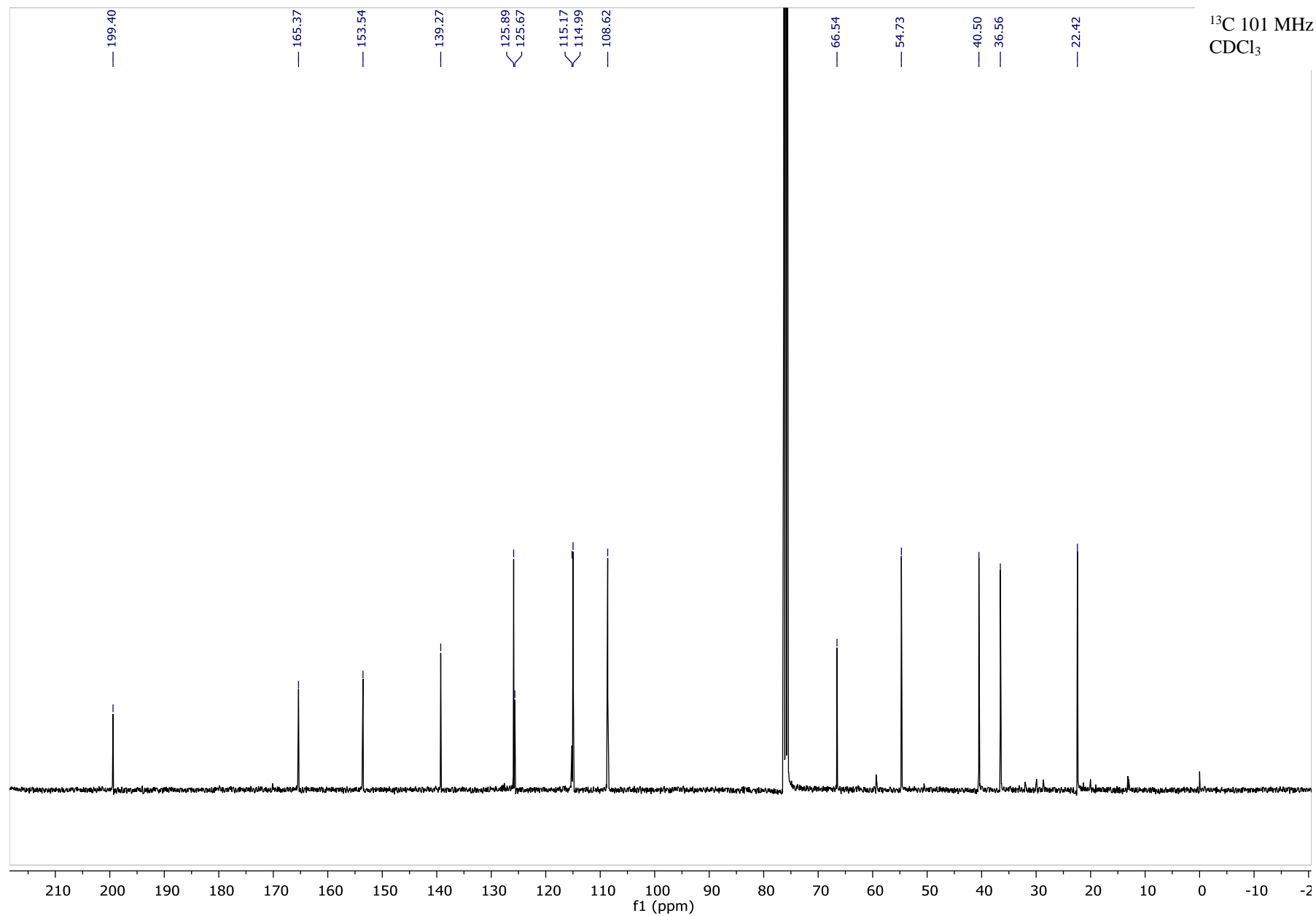


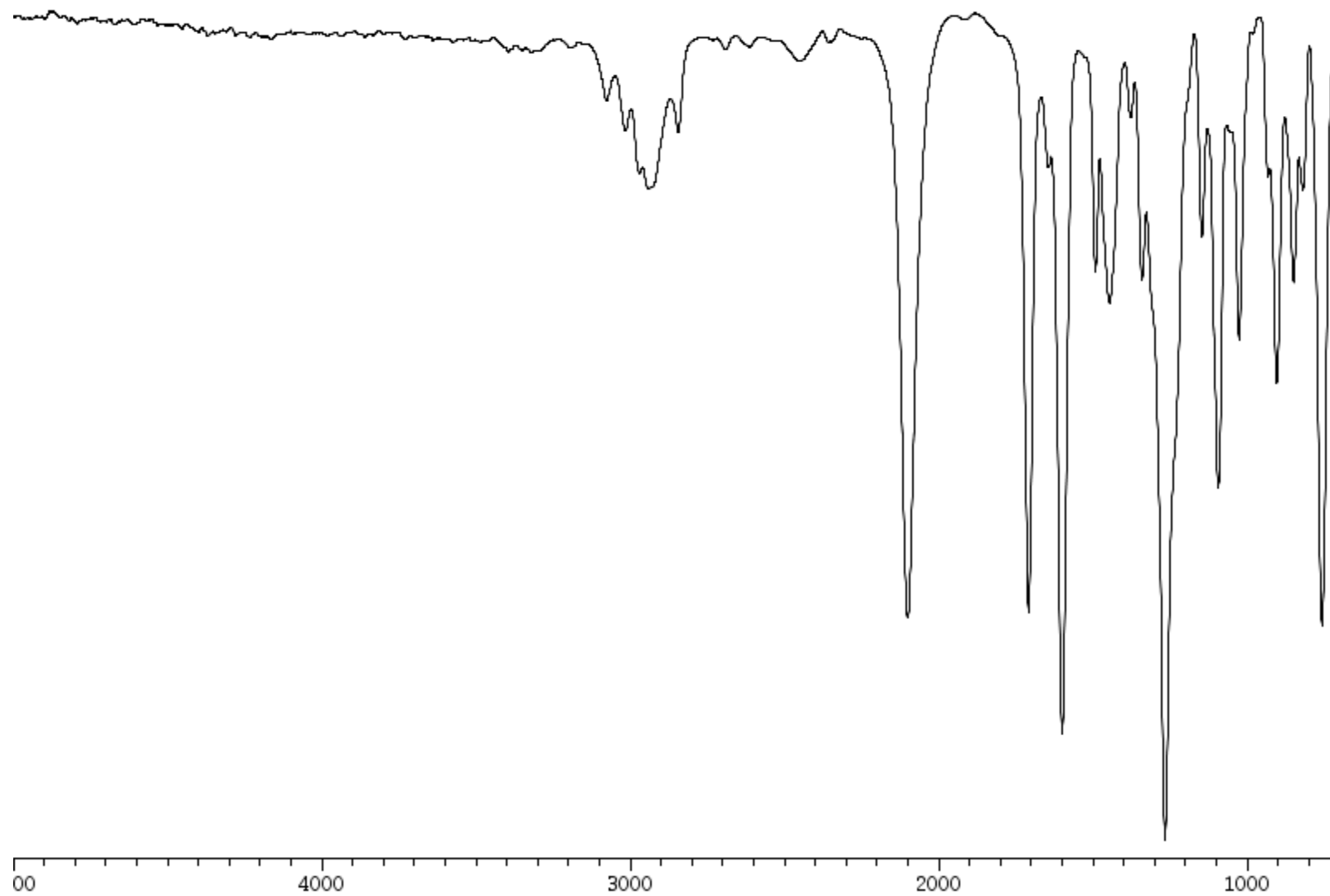
| # | Peak Name | CH | tR | Area | Height | Area% | Height% | Quantity | NTP | Resolution | Symmetry Factor | Warning |
|---|-----------|----|--------|---------|--------|--------|---------|----------|-------|------------|-----------------|---------|
| 1 | Unknown | 2 | 8.950 | 594863 | 50747 | 6.662 | 7.544 | N/A | 14349 | 4.911 | 1.230 | |
| 2 | Unknown | 2 | 10.517 | 8334632 | 621978 | 93.338 | 92.456 | N/A | 15233 | N/A | 1.235 | |

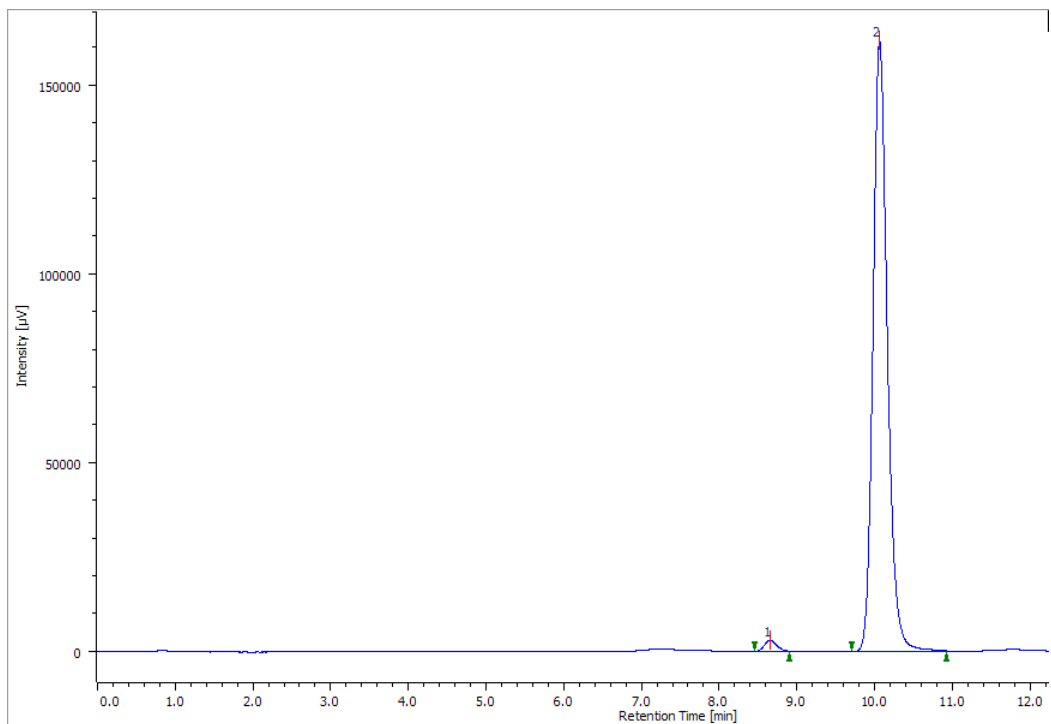


| # | Peak Name | CH | tR | Area | Height | Area% | Height% | Quantity | NTP | Resolution | Symmetry Factor | Warning |
|---|-----------|----|--------|-------|--------|--------|---------|----------|-------|------------|-----------------|---------|
| 1 | Unknown | 2 | 8.963 | 83934 | 7110 | 49.230 | 52.788 | N/A | 14117 | 4.902 | 1.169 | |
| 2 | Unknown | 2 | 10.547 | 86580 | 6359 | 50.770 | 47.212 | N/A | 14874 | N/A | 1.169 | |

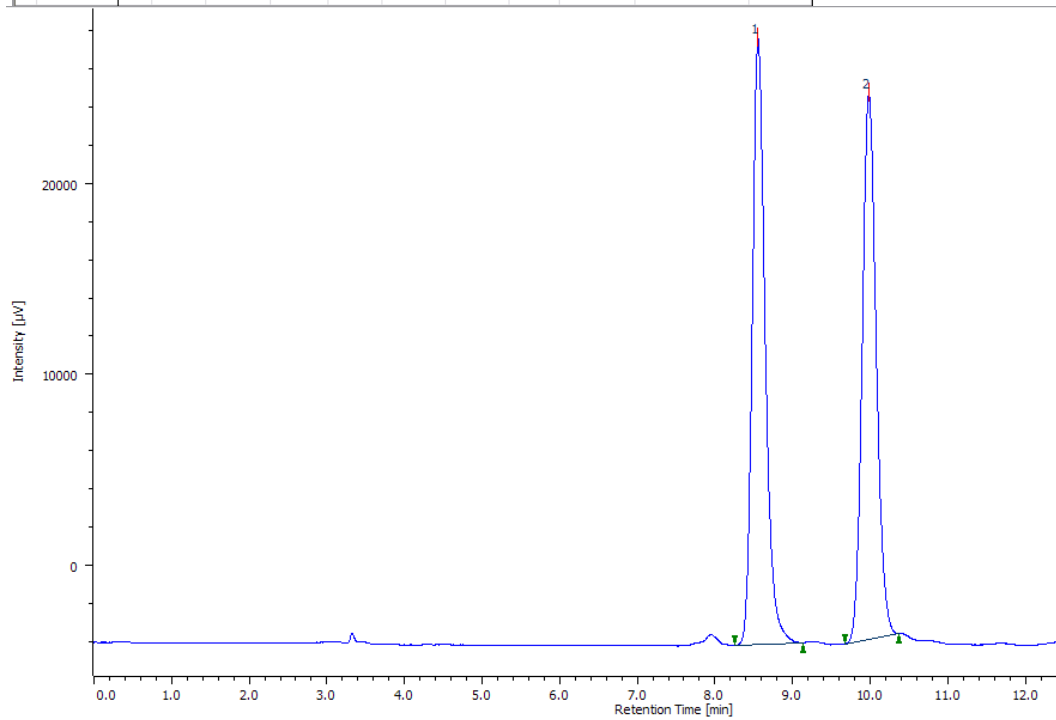




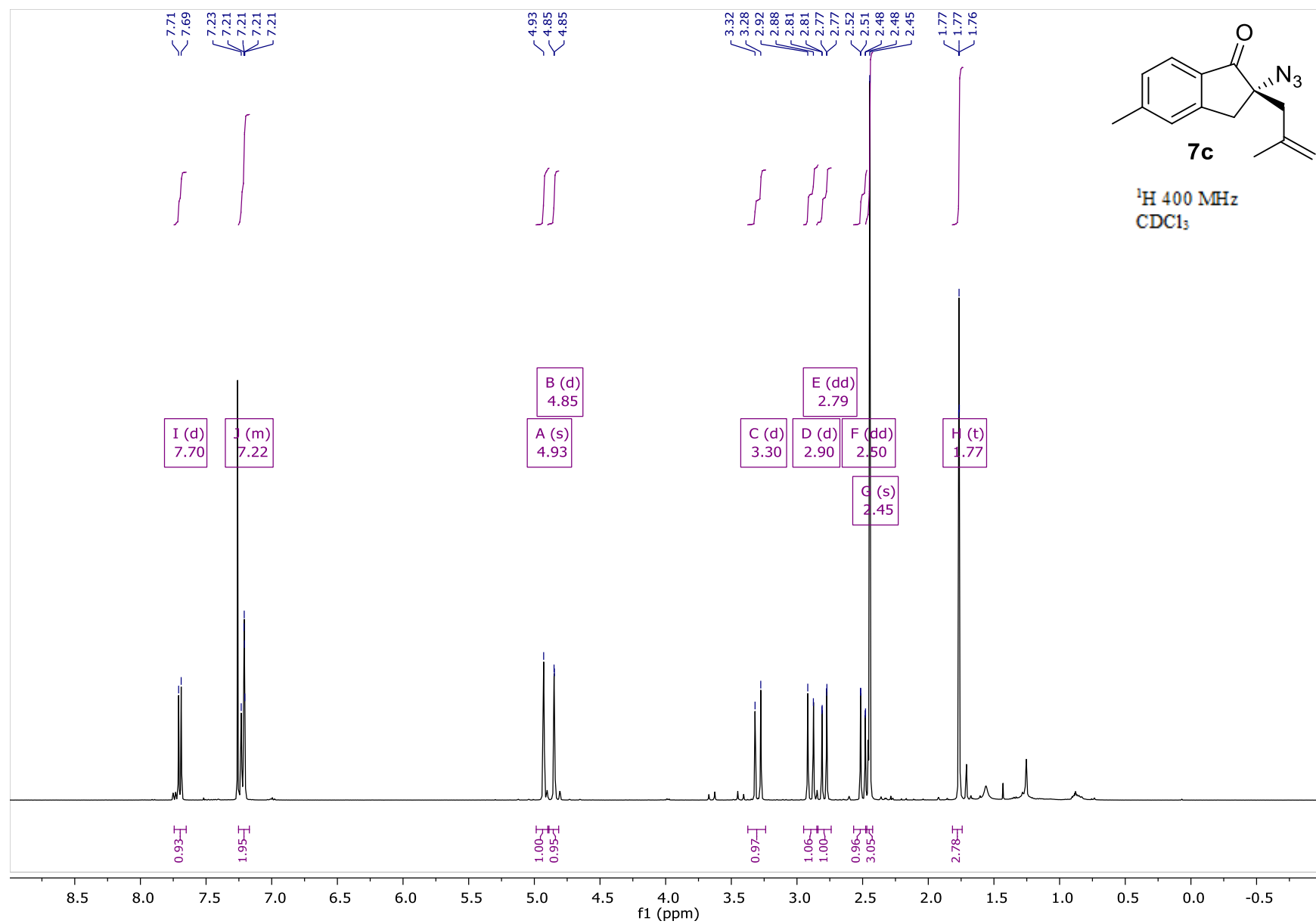


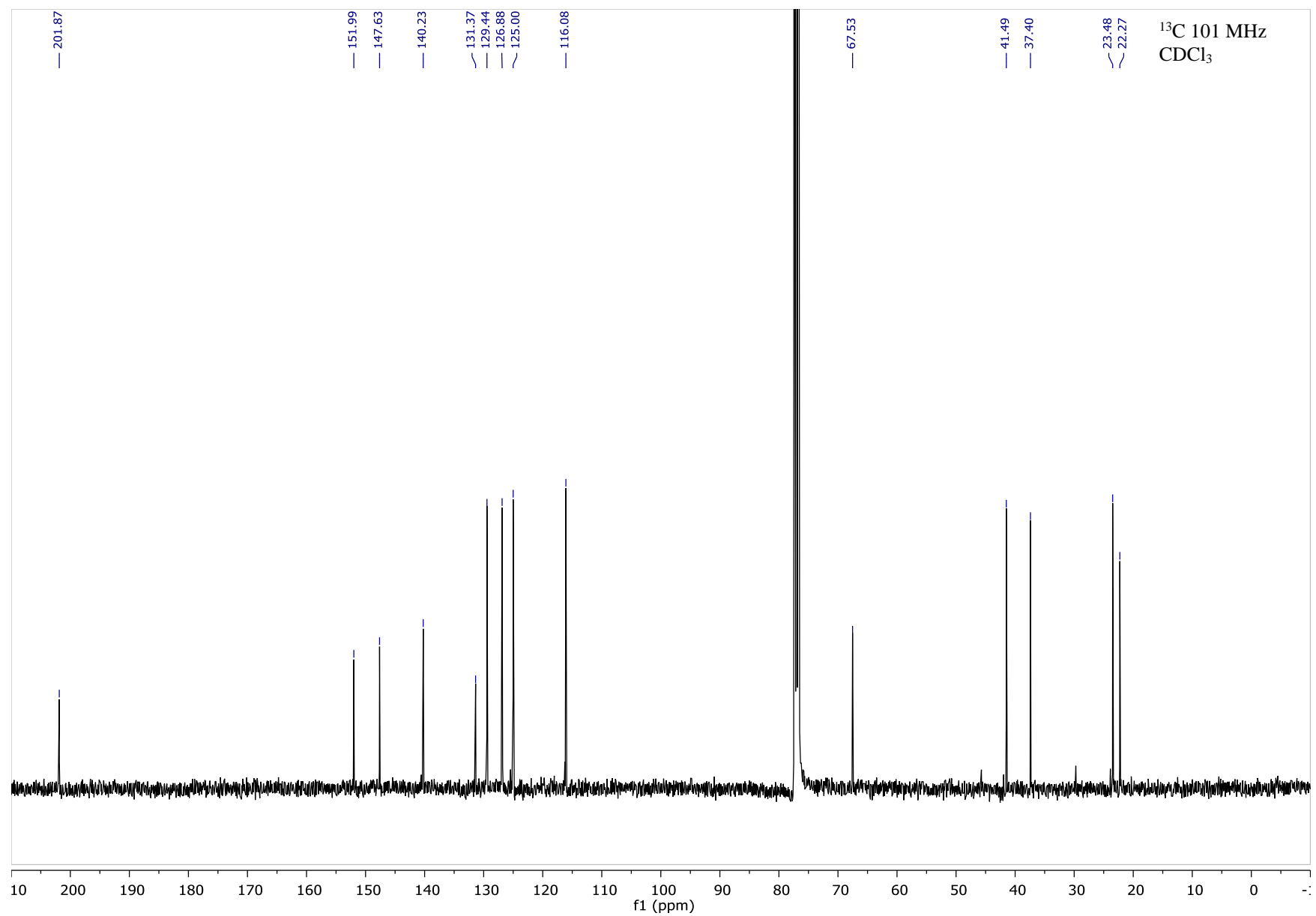


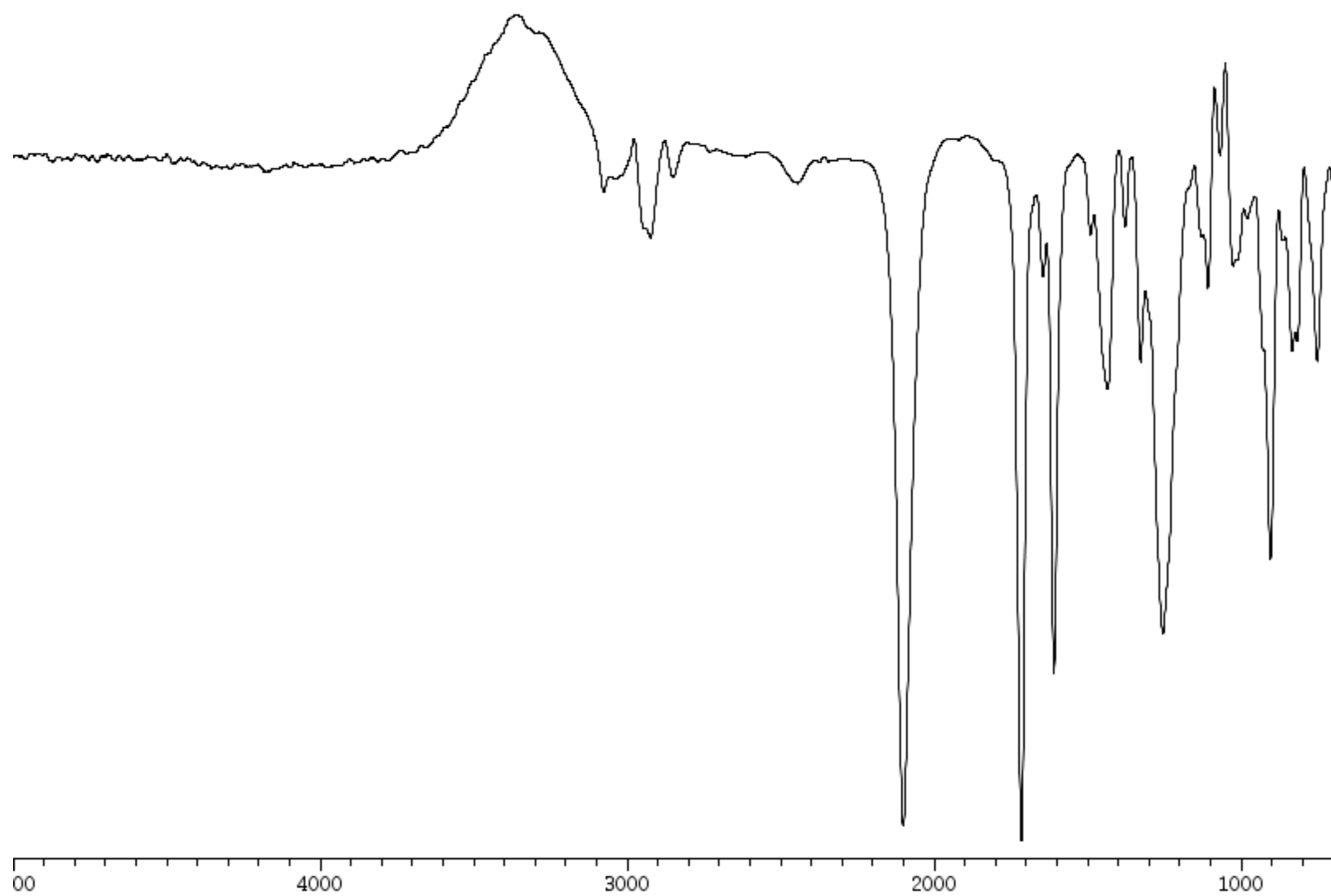
| # | Peak Name | CH | tR | Area | Height | Area% | Height% | Quantity | NTP | Resolution | Symmetry Factor | Warning |
|---|-----------|----|--------|---------|--------|--------|---------|----------|-------|------------|-----------------|---------|
| 1 | Unknown | 1 | 8.647 | 31586 | 2917 | 1.508 | 1.775 | N/A | 14601 | 4.618 | 1.147 | |
| 2 | Unknown | 1 | 10.053 | 2062924 | 161365 | 98.492 | 98.225 | N/A | 15342 | N/A | 1.208 | |

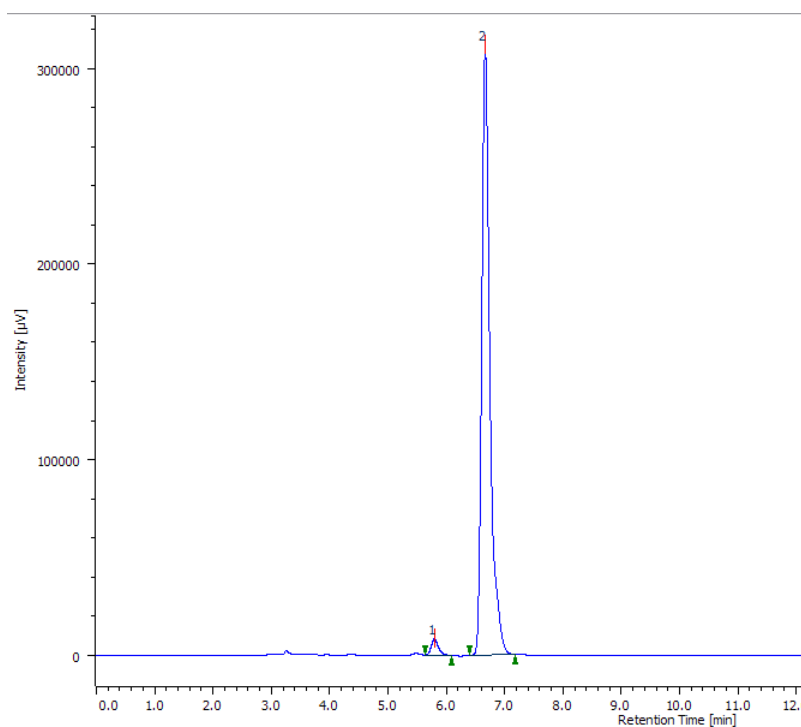


| # | Peak Name | CH | tR | Area | Height | Area% | Height% | Quantity | NTP | Resolution | Symmetry Factor | Warning |
|---|-----------|----|-------|--------|--------|--------|---------|----------|-------|------------|-----------------|---------|
| 1 | Unknown | 1 | 8.547 | 367337 | 31695 | 50.711 | 52.571 | N/A | 13656 | 4.635 | 1.263 | |
| 2 | Unknown | 1 | 9.973 | 357038 | 28596 | 49.289 | 47.429 | N/A | 15097 | N/A | 1.132 | |

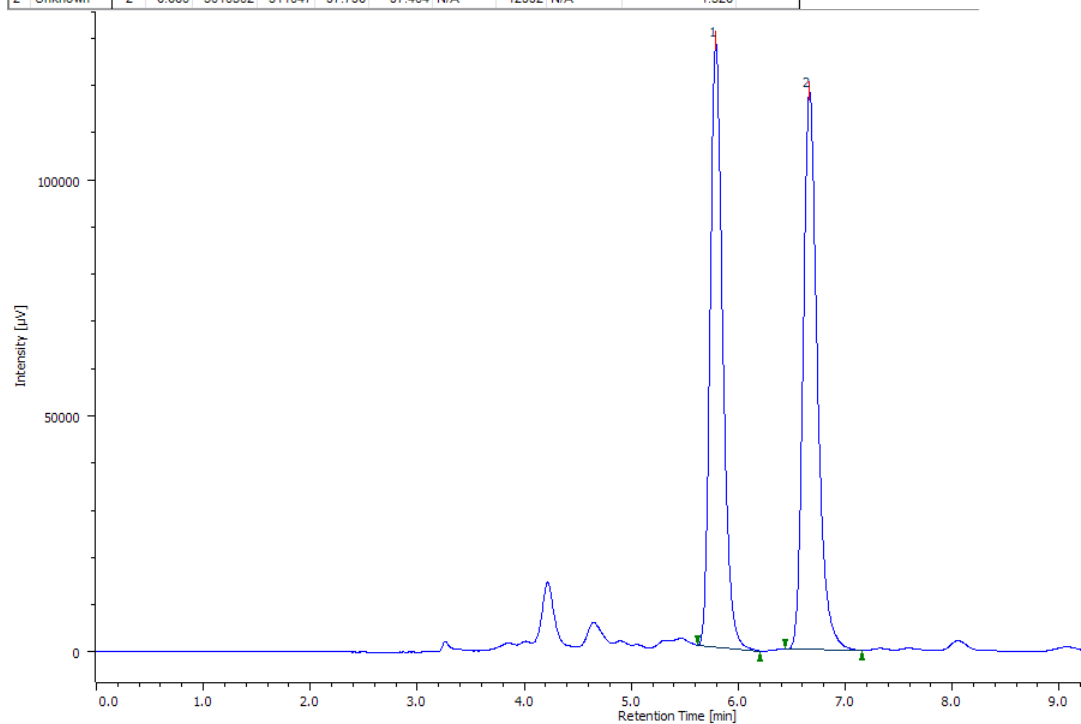




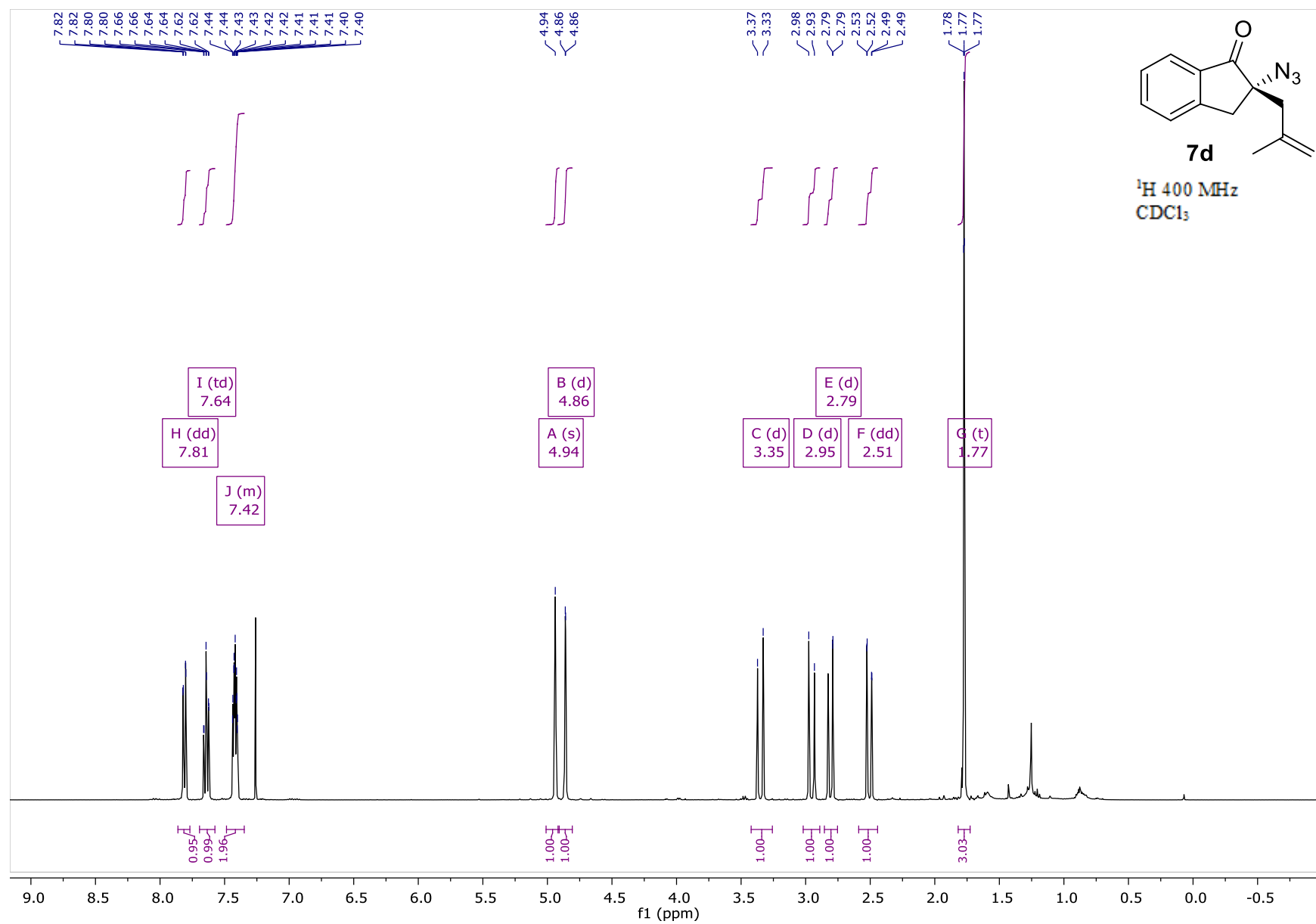


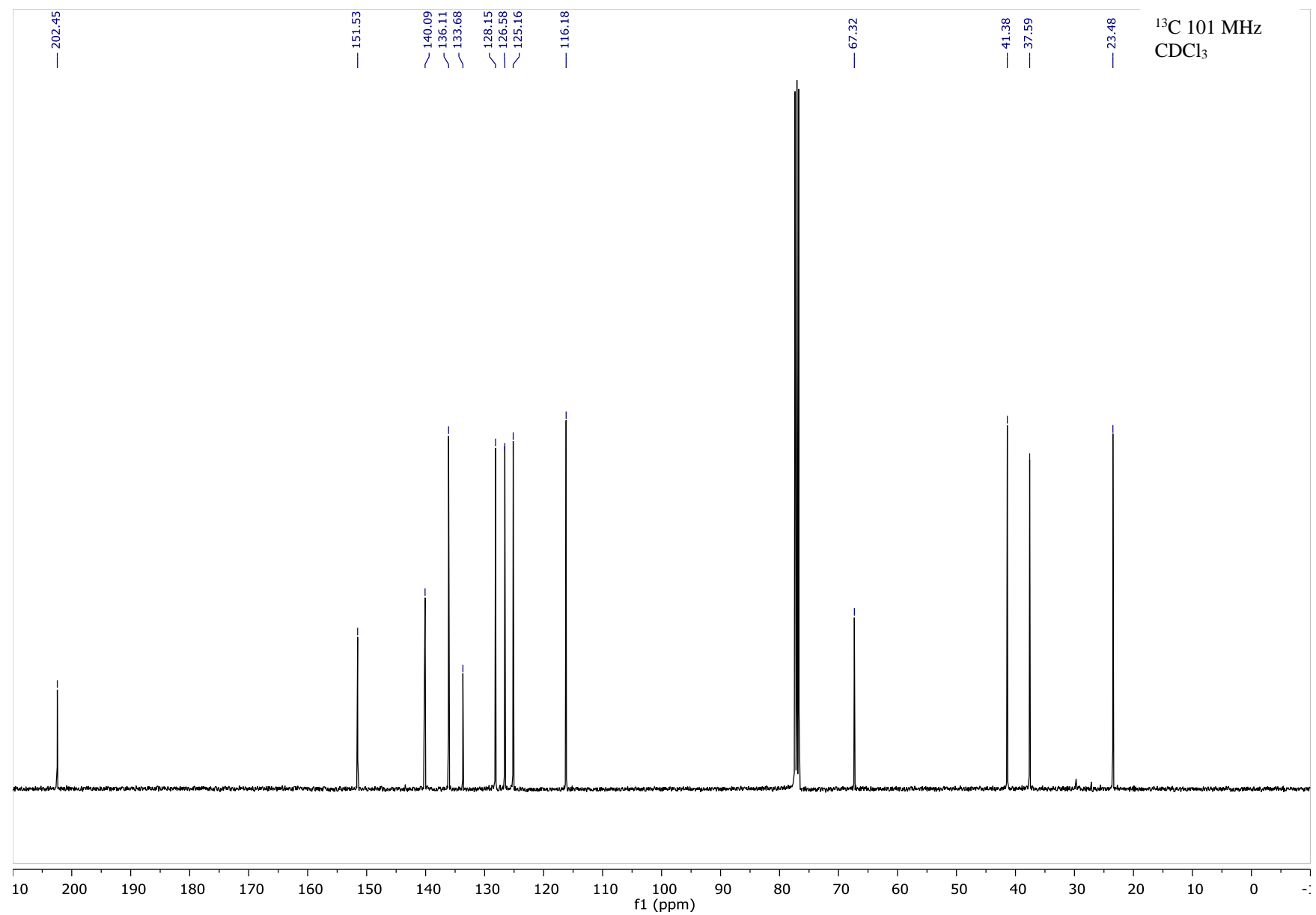


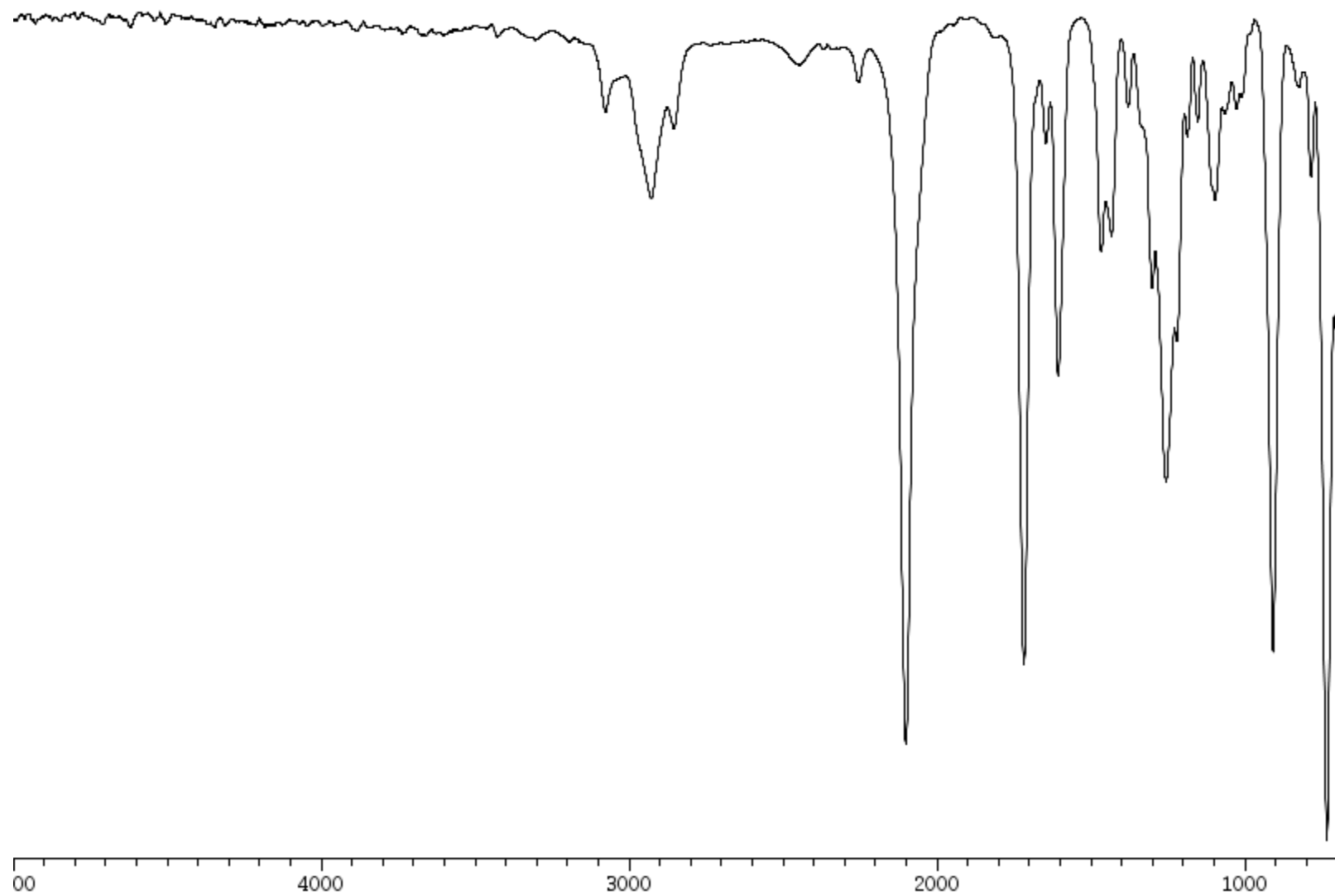
| # | Peak Name | CH | IR | Area | Height | Area% | Height% | Quantity | NTP | Resolution | Symmetry Factor | Warning |
|---|-----------|----|-------|---------|--------|--------|---------|----------|-------|------------|-----------------|---------|
| 1 | Unknown | 2 | 5.790 | 67832 | 8289 | 2.204 | 2.596 | N/A | 11986 | 3.918 | 1.239 | |
| 2 | Unknown | 2 | 6.660 | 3010502 | 311047 | 97.796 | 97.404 | N/A | 12992 | N/A | 1.526 | |

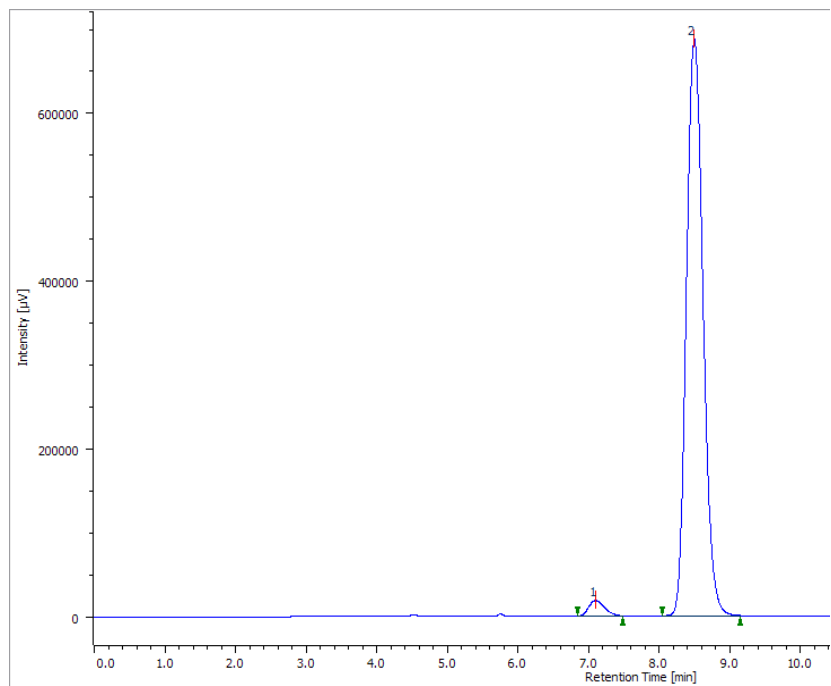


| # | Peak Name | CH | IR | Area | Height | Area% | Height% | Quantity | NTP | Resolution | Symmetry Factor | Warning |
|---|-----------|----|-------|---------|--------|--------|---------|----------|-------|------------|-----------------|---------|
| 1 | Unknown | 2 | 5.783 | 1051422 | 128098 | 49.027 | 52.039 | N/A | 12058 | 3.957 | 1.260 | |
| 2 | Unknown | 2 | 6.660 | 1093154 | 118060 | 50.973 | 47.961 | N/A | 13006 | N/A | 1.290 | |

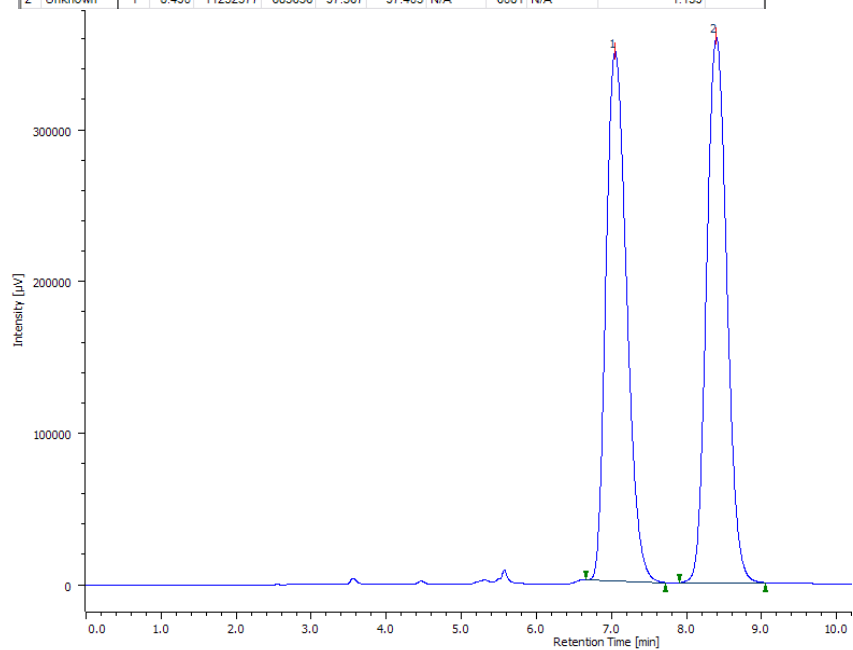




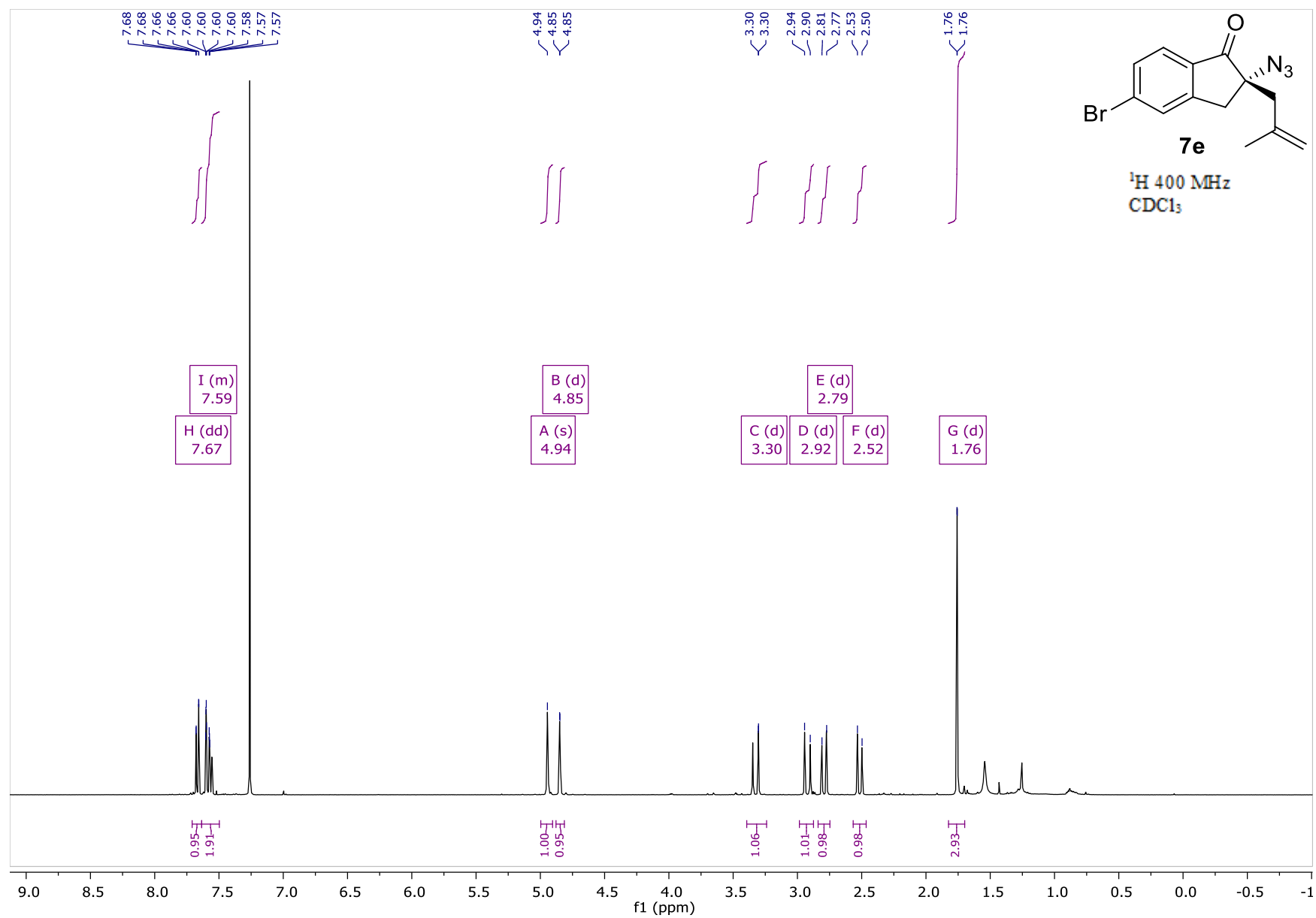


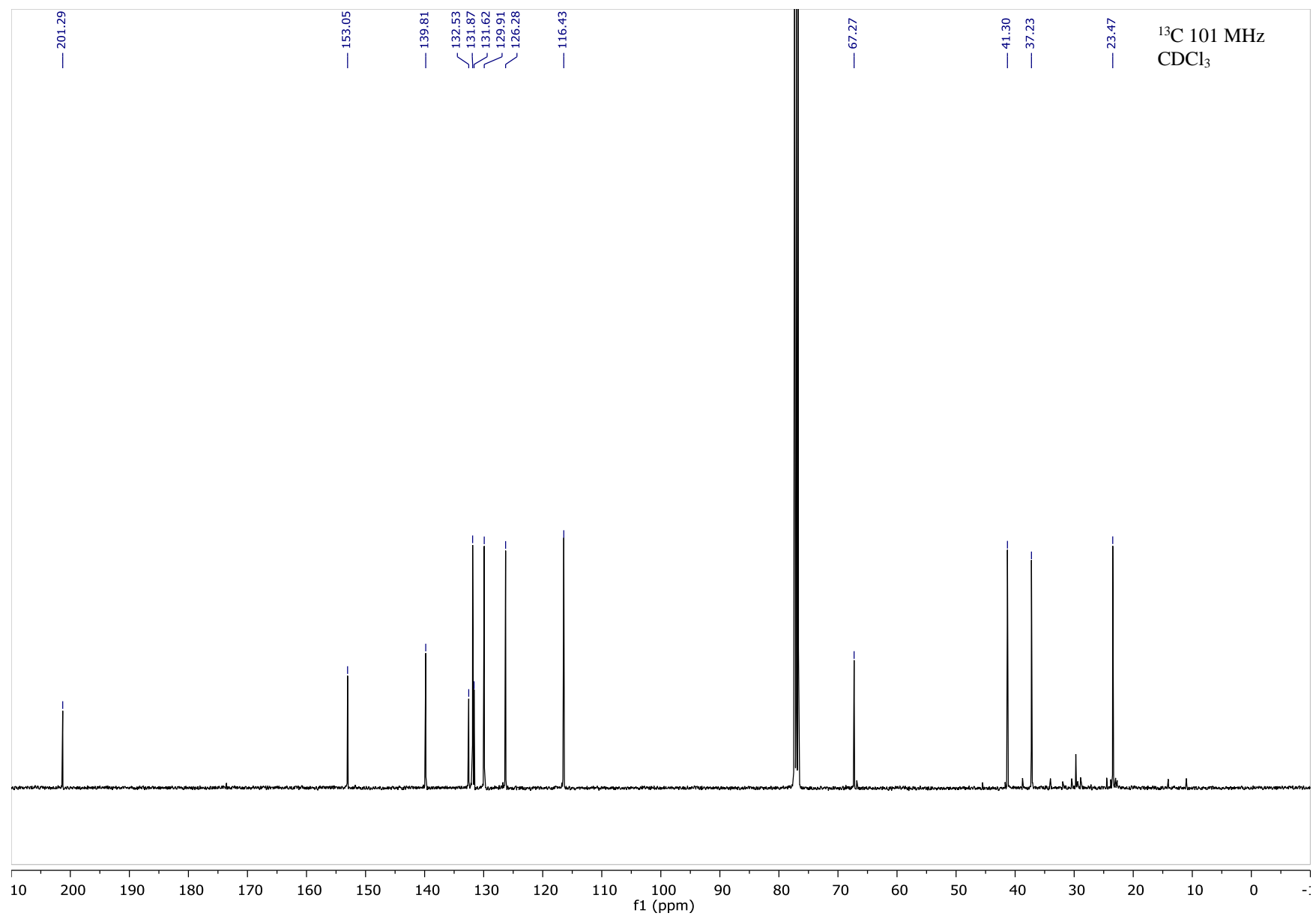


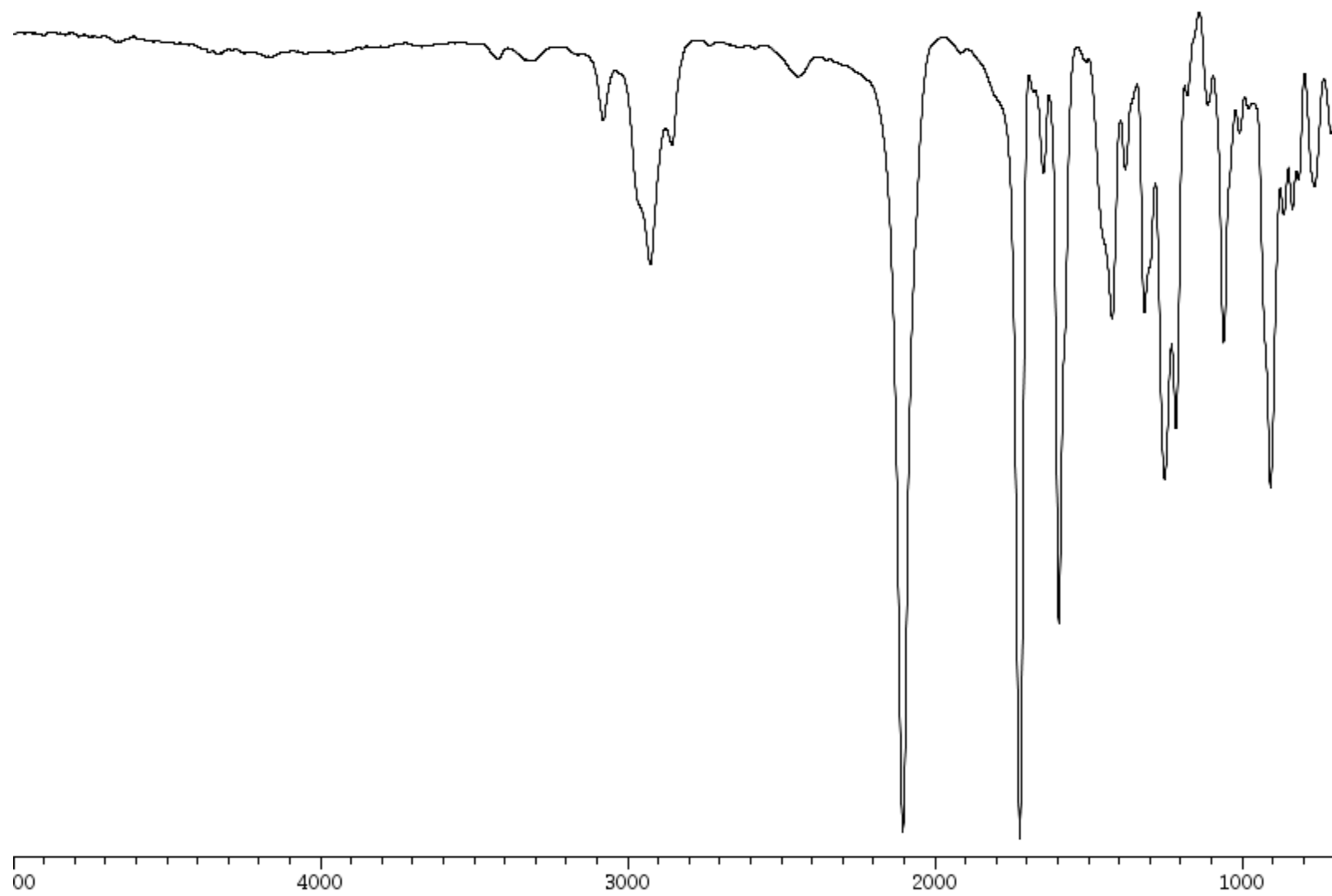
| # | Peak Name | CH | tR | Area | Height | Area% | Height% | Quantity | NTP | Resolution | Symmetry Factor | Warning |
|---|-----------|----|-------|----------|--------|--------|---------|----------|------|------------|-----------------|---------|
| 1 | Unknown | 1 | 7.093 | 280639 | 18283 | 2.433 | 2.597 | N/A | 4881 | 3.328 | 1.294 | |
| 2 | Unknown | 1 | 8.490 | 11262377 | 685636 | 97.567 | 97.403 | N/A | 6081 | N/A | 1.159 | |

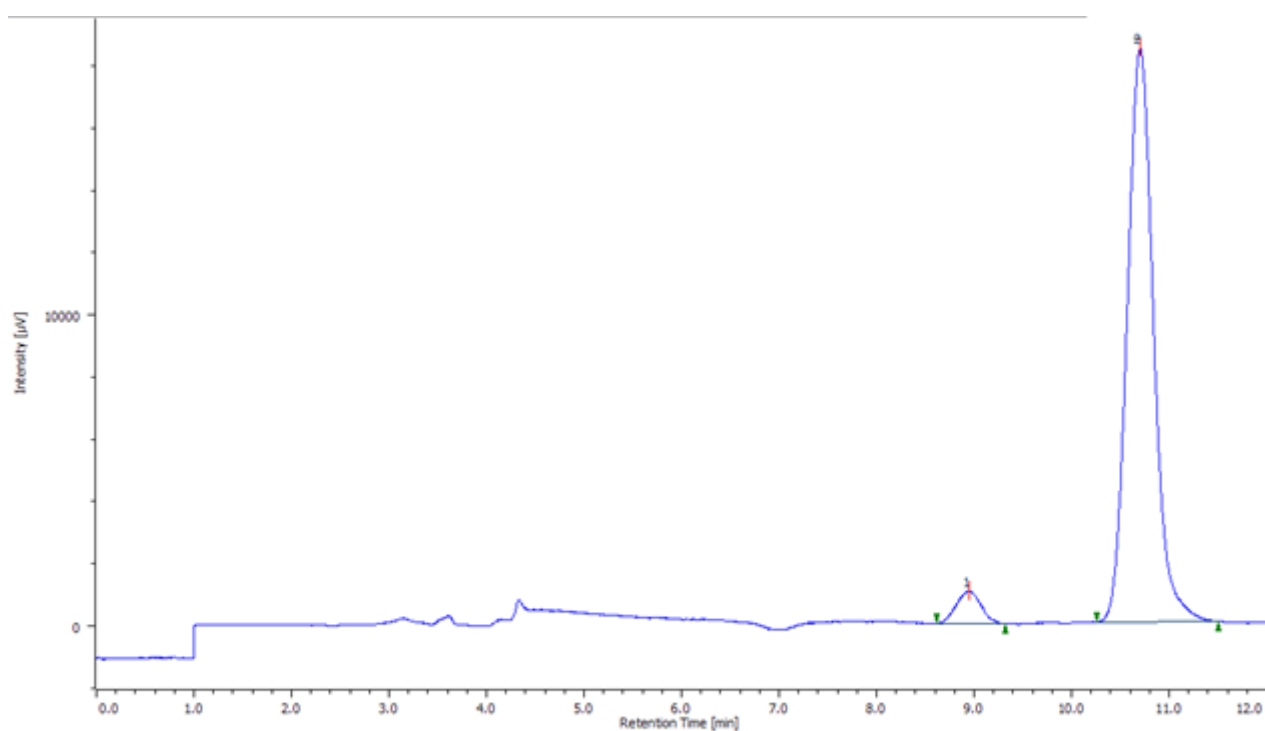


| # | Peak Name | CH | tR | Area | Height | Area% | Height% | Quantity | NTP | Resolution | Symmetry Factor | Warning |
|---|-----------|----|-------|---------|--------|--------|---------|----------|------|------------|-----------------|---------|
| 1 | Unknown | 1 | 7.040 | 6645127 | 348483 | 49.586 | 49.234 | N/A | 3041 | 2.673 | 1.270 | |
| 2 | Unknown | 1 | 8.390 | 6756978 | 359329 | 50.414 | 50.766 | N/A | 4467 | N/A | 1.108 | |

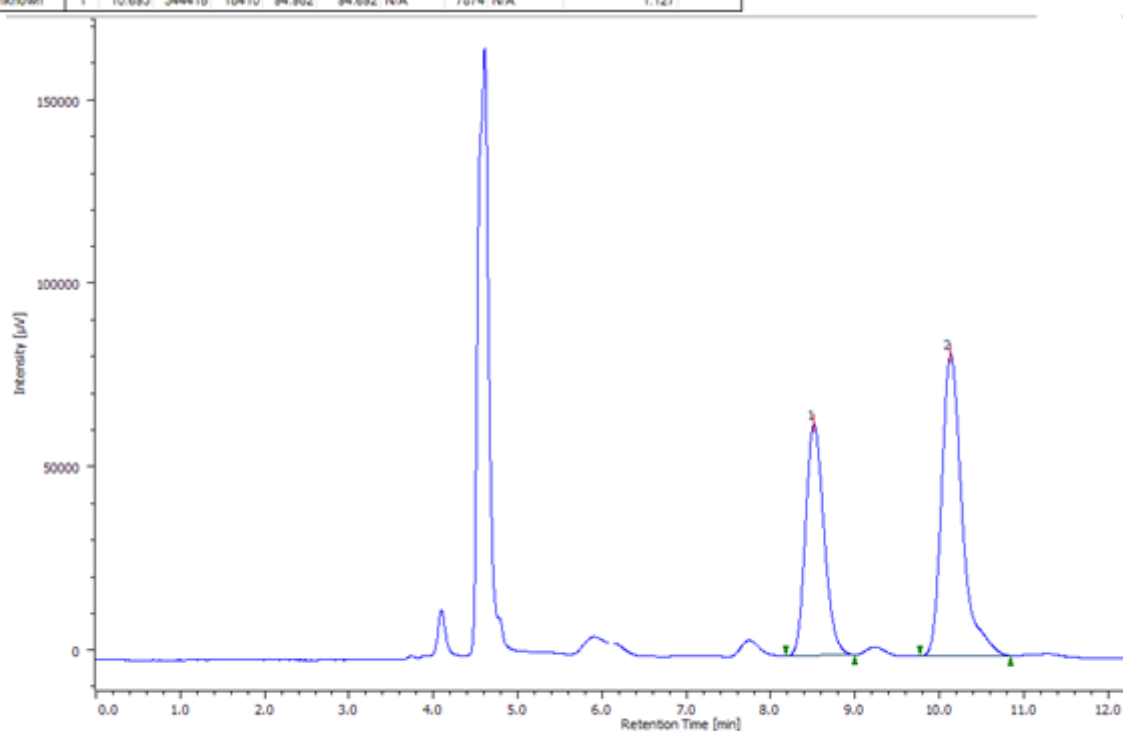




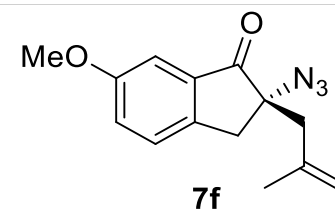




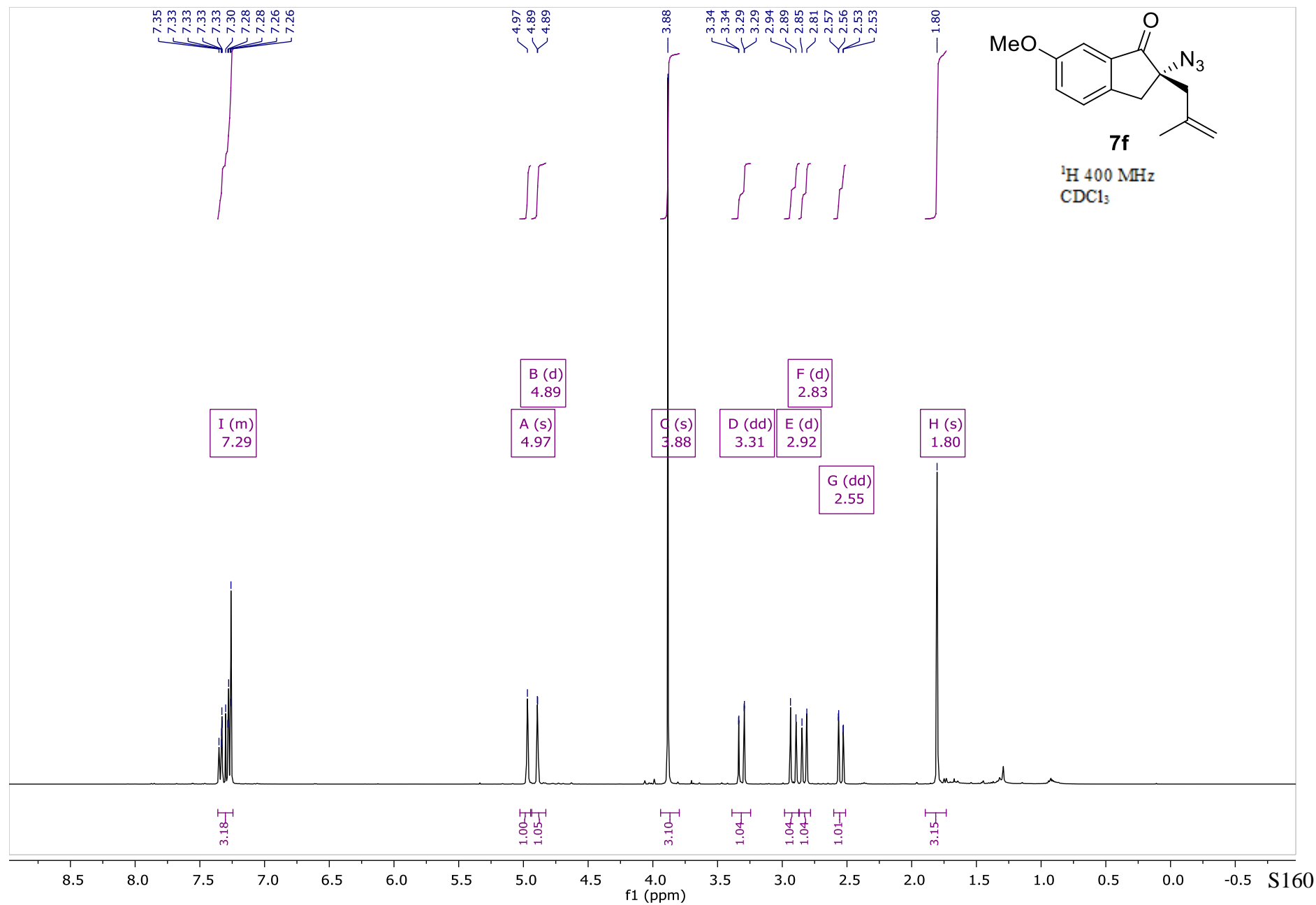
| # | Peak Name | CH | IR | Area | Height | Area% | Height% | Quantity | NTP | Resolution | Symmetry Factor | Warning |
|---|-----------|----|--------|--------|--------|--------|---------|----------|------|------------|-----------------|---------|
| 1 | Unknown | 1 | 8.940 | 18196 | 1032 | 5.018 | 5.308 | N/A | 5471 | 3.642 | 1.043 | |
| 2 | Unknown | 1 | 10.693 | 344415 | 18410 | 94.982 | 94.692 | N/A | 7874 | N/A | 1.127 | |

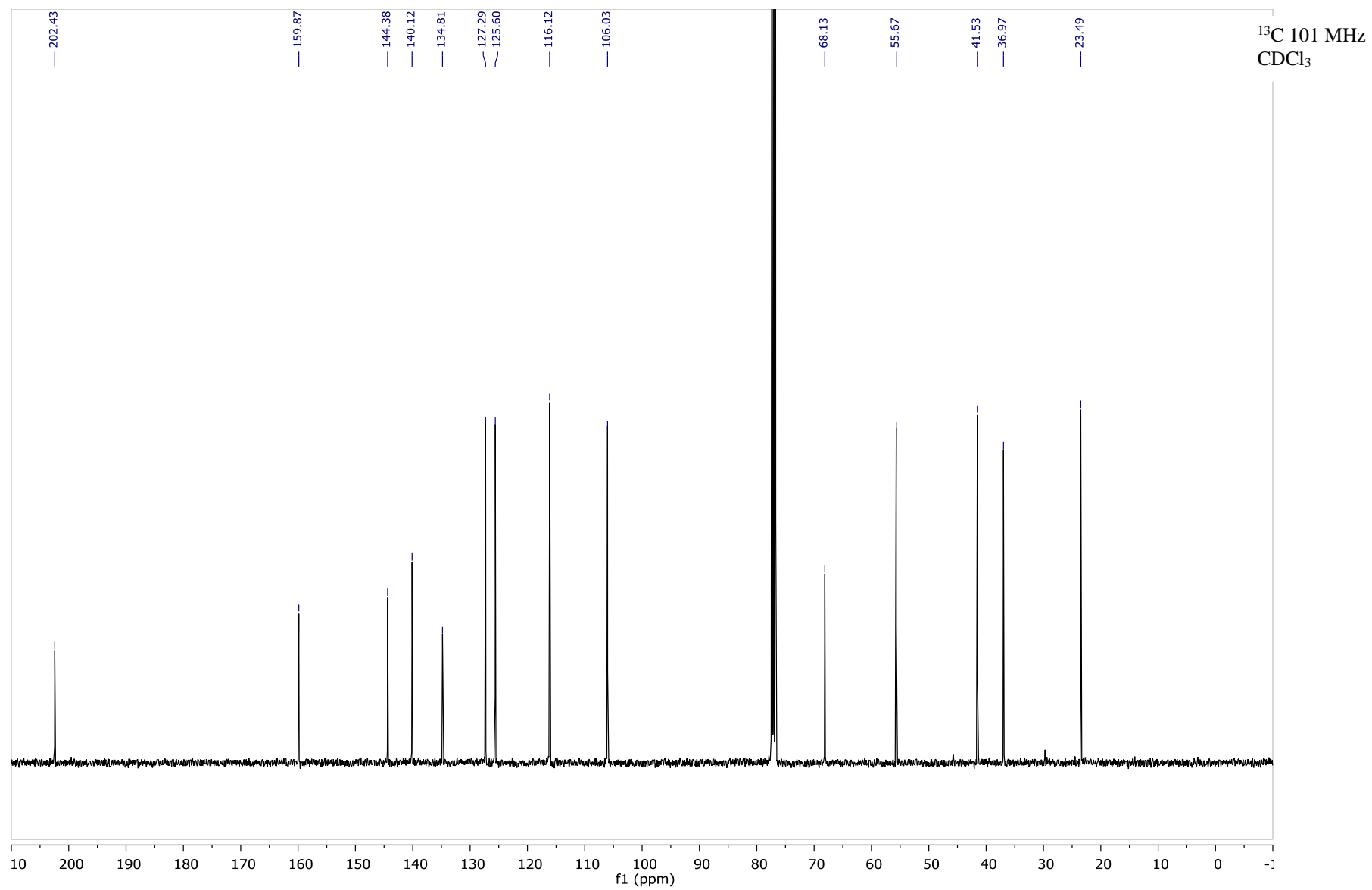


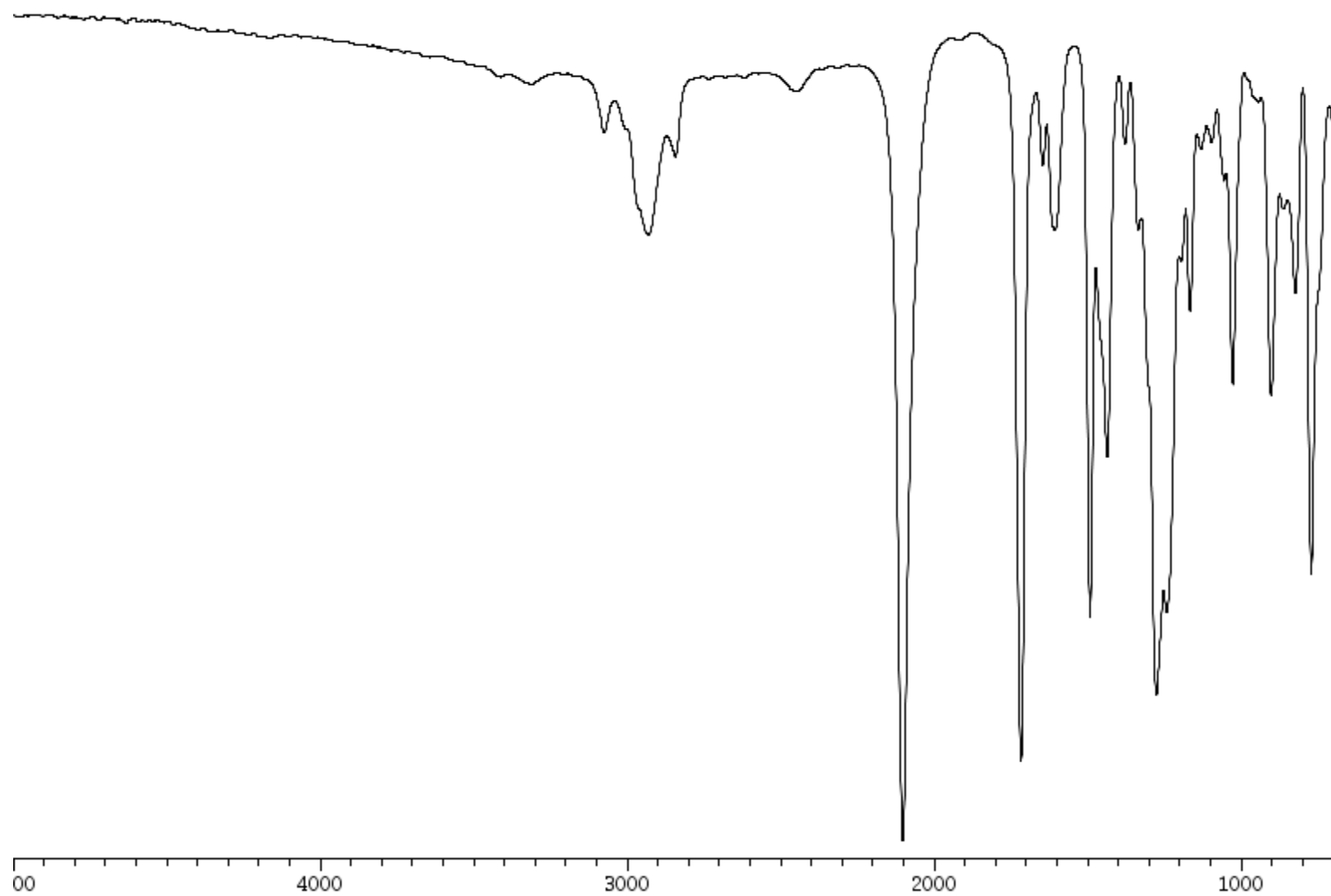
| # | Peak Name | CH | IR | Area | Height | Area% | Height% | Quantity | NTP | Resolution | Symmetry Factor | Warning |
|---|-----------|----|--------|---------|--------|--------|---------|----------|------|------------|-----------------|---------|
| 1 | Unknown | 1 | 8.603 | 961743 | 63202 | 40.939 | 43.484 | N/A | 7242 | 3.977 | 1.207 | |
| 2 | Unknown | 1 | 10.123 | 1387487 | 82141 | 59.061 | 56.516 | N/A | 9426 | N/A | 1.490 | |

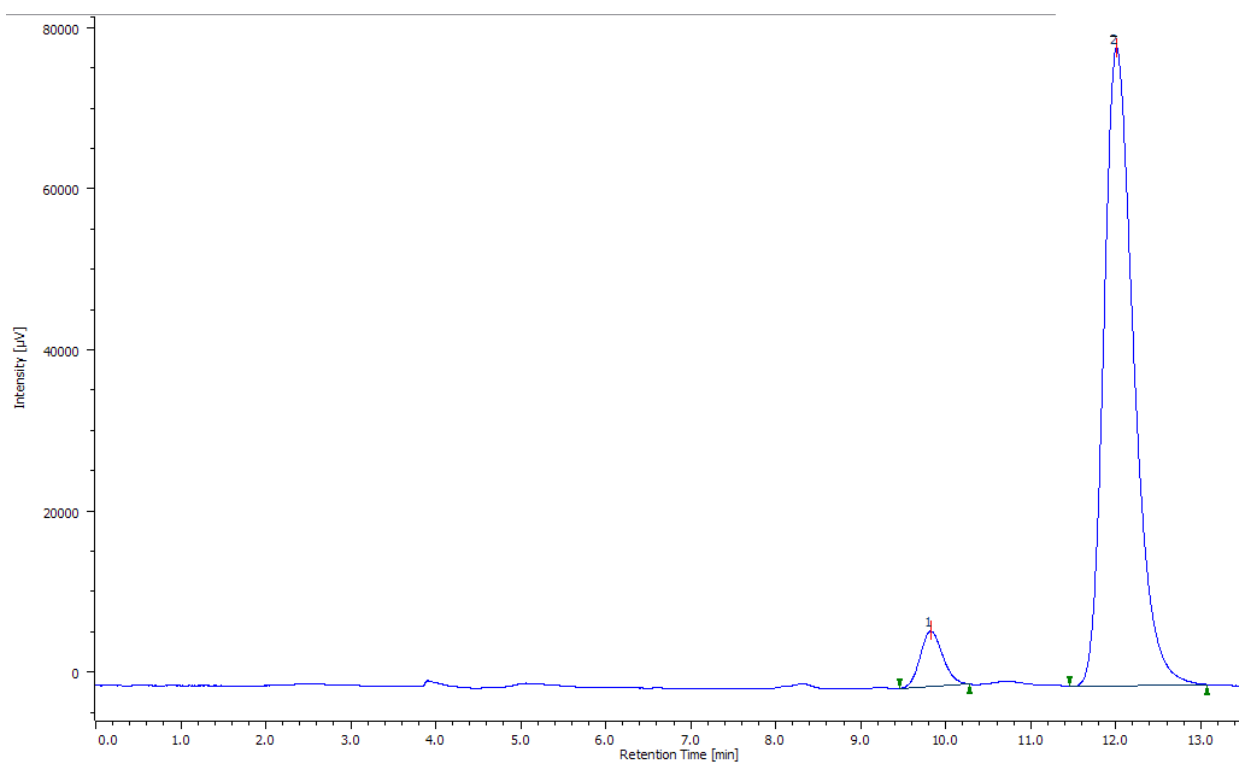


^1H 400 MHz
 CDCl_3

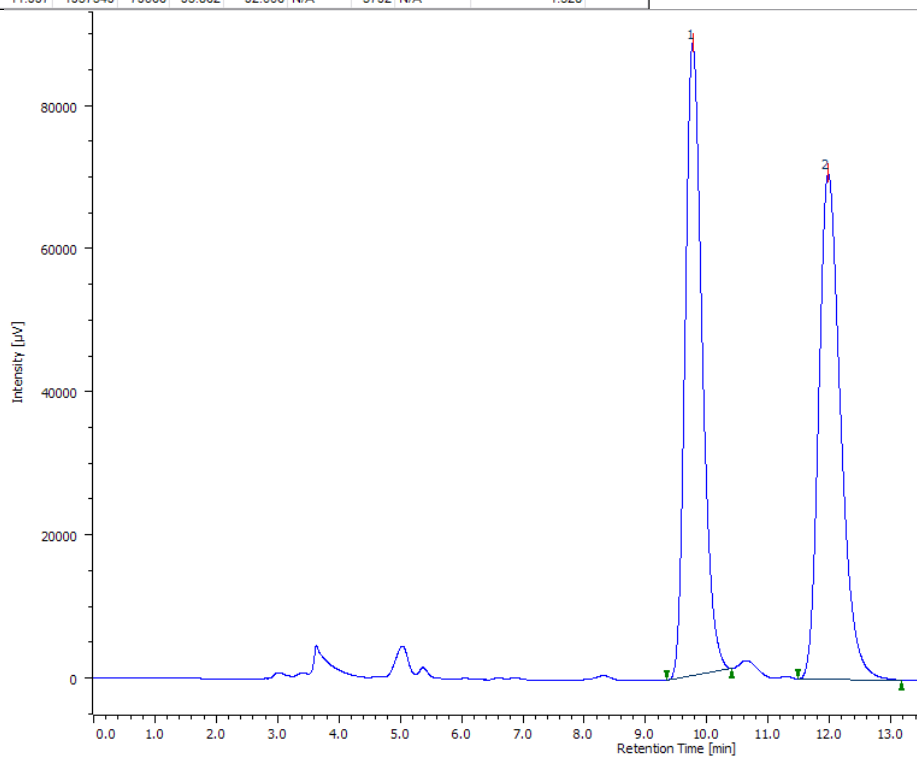




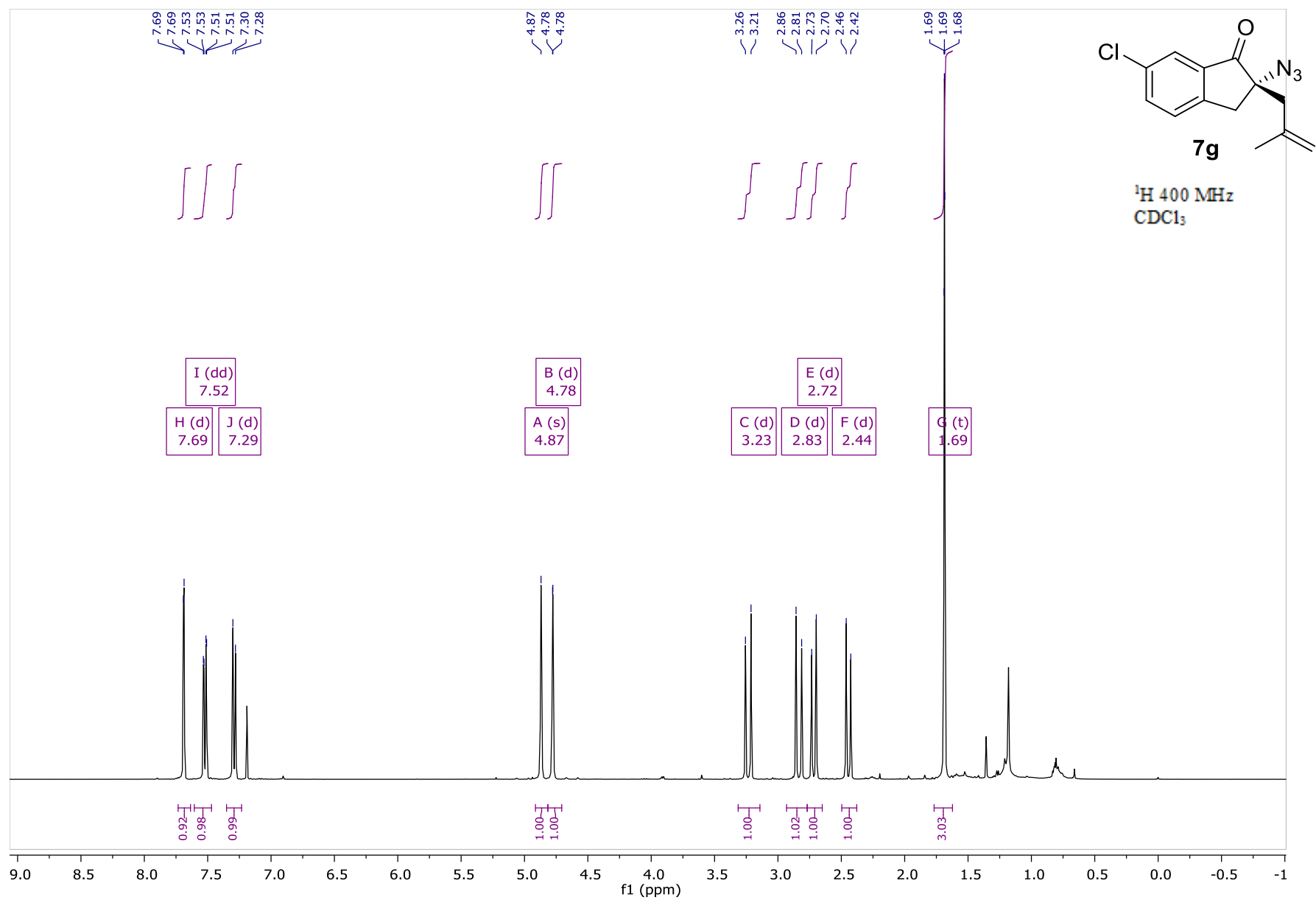


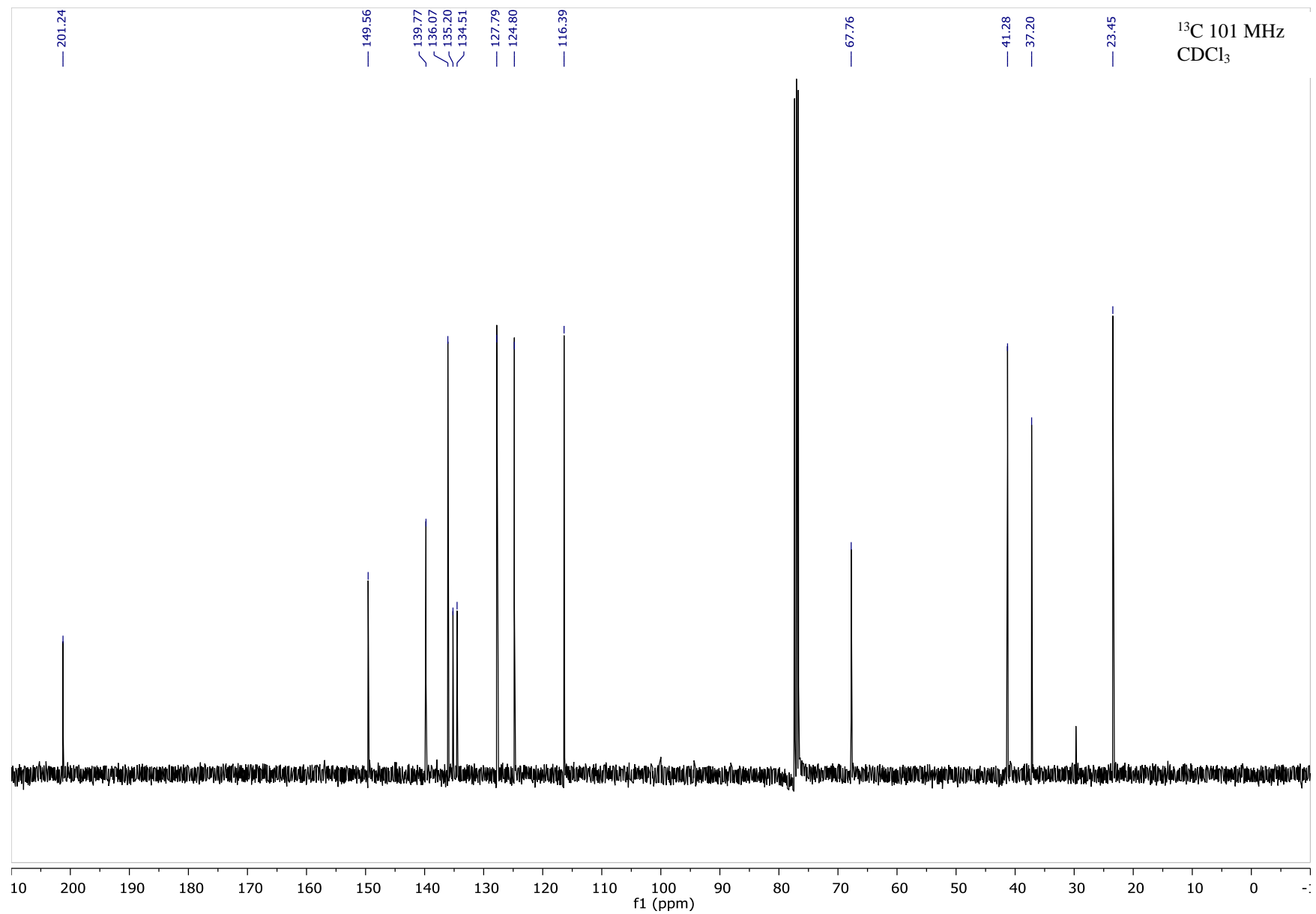


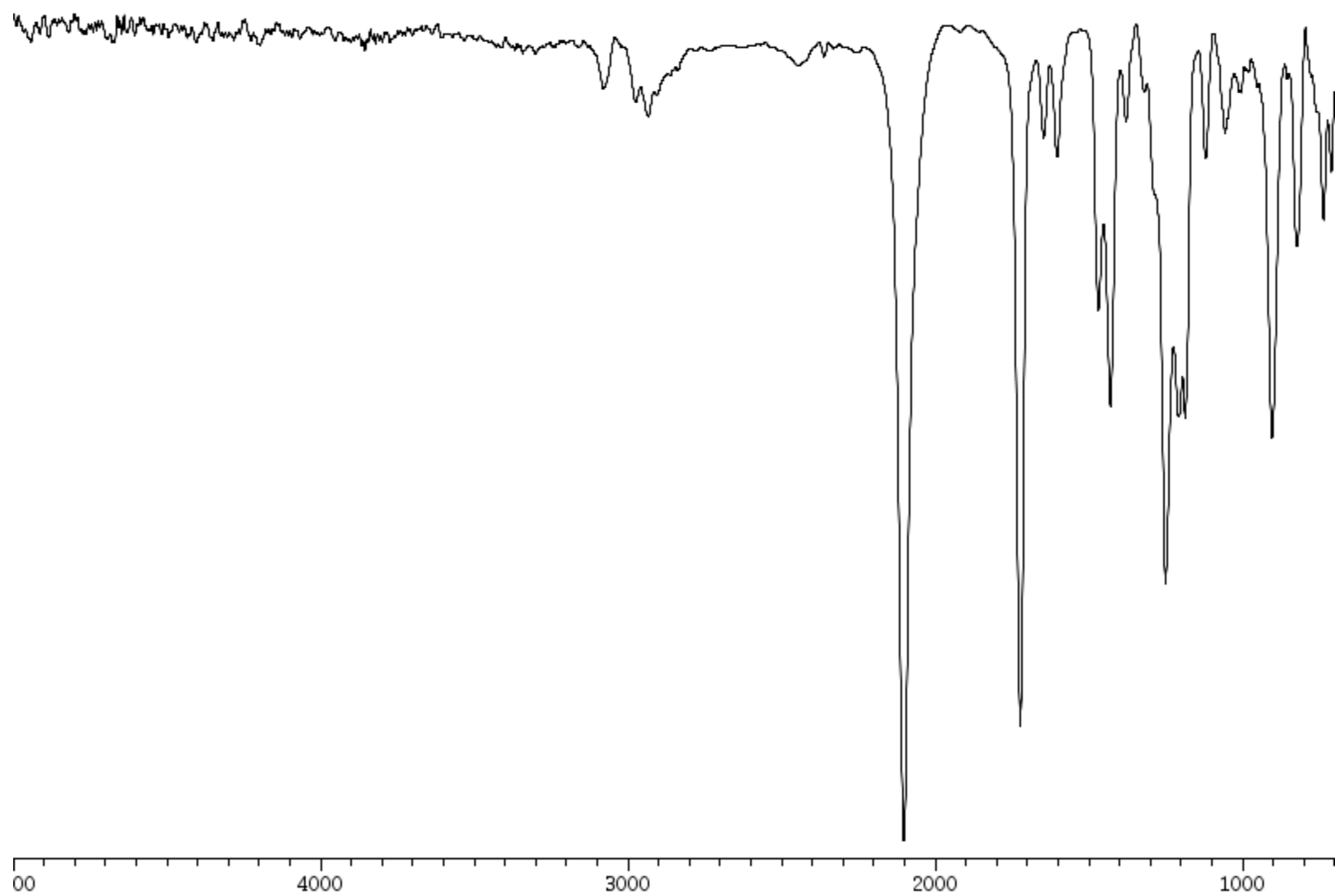
| # | Peak Name | CH | tR | Area | Height | Area% | Height% | Quantity | NTP | Resolution | Symmetry Factor | Warning |
|---|-----------|----|--------|---------|--------|--------|---------|----------|------|------------|-----------------|---------|
| 1 | Unknown | 1 | 9.817 | 126699 | 6869 | 6.138 | 7.994 | N/A | 6541 | 3.917 | 1.156 | |
| 2 | Unknown | 1 | 11.997 | 1937349 | 79066 | 93.862 | 92.006 | N/A | 5792 | N/A | 1.328 | |

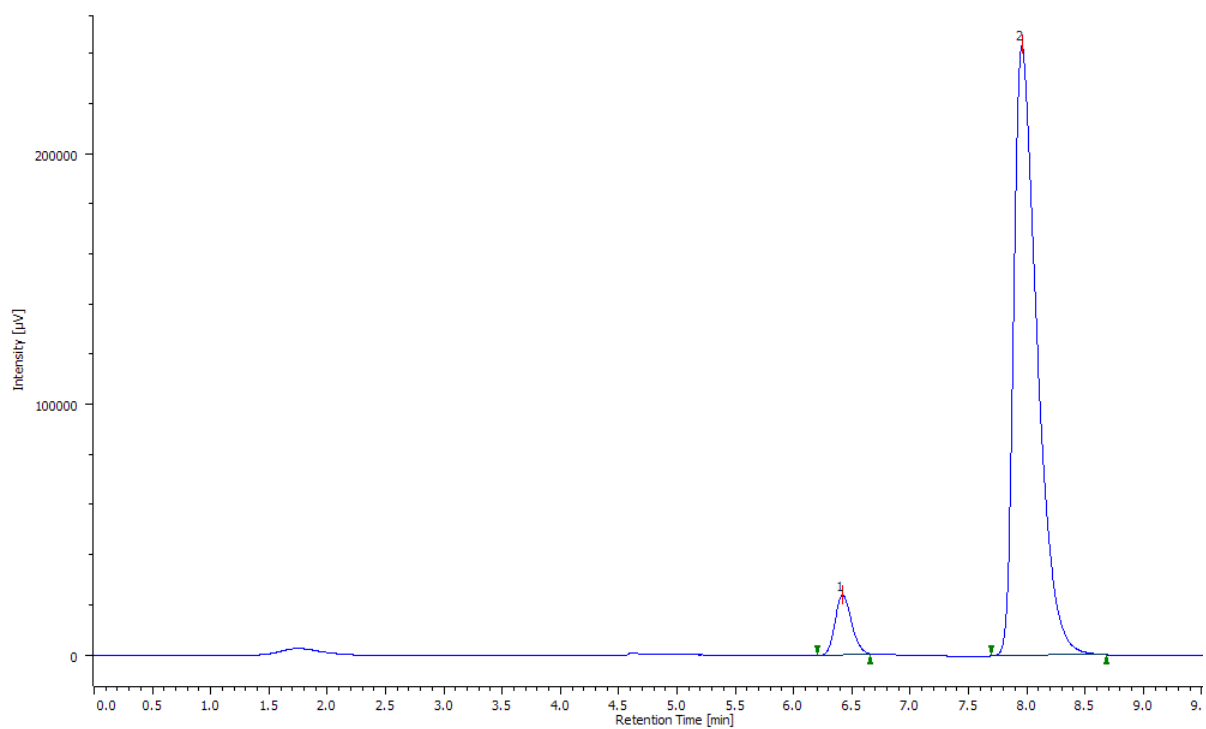


| # | Peak Name | CH | tR | Area | Height | Area% | Height% | Quantity | NTP | Resolution | Symmetry Factor | Warning |
|---|-----------|----|--------|---------|--------|--------|---------|----------|------|------------|-----------------|---------|
| 1 | Unknown | 1 | 9.760 | 1698027 | 88297 | 49.326 | 55.580 | N/A | 6101 | 3.891 | 1.265 | |
| 2 | Unknown | 1 | 11.967 | 1744442 | 70569 | 50.674 | 44.420 | N/A | 5638 | N/A | 1.309 | |

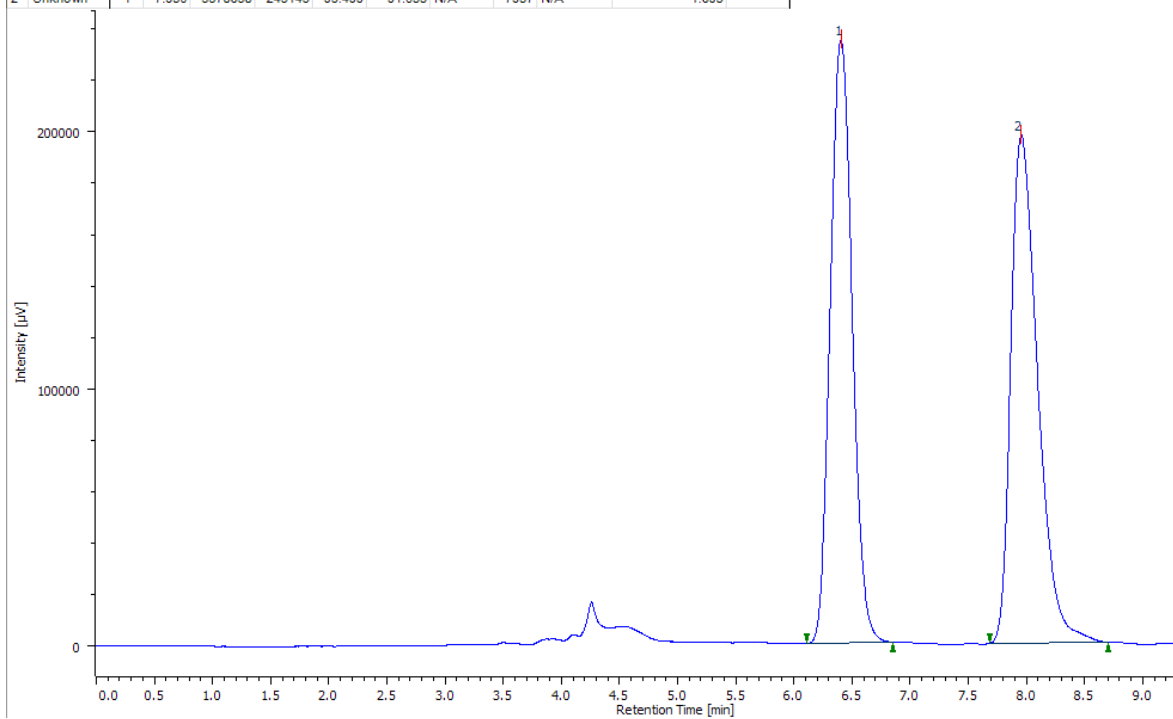




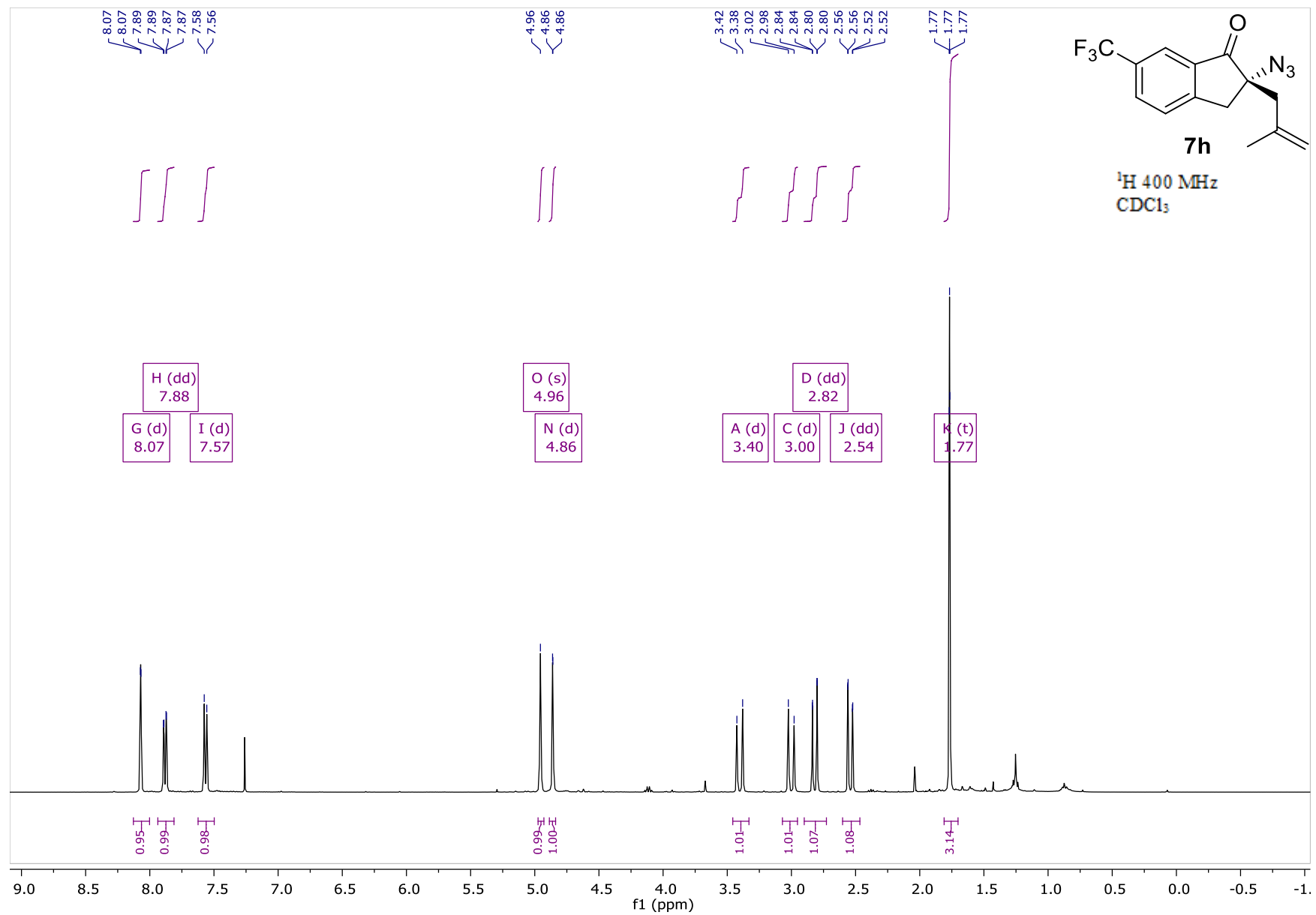


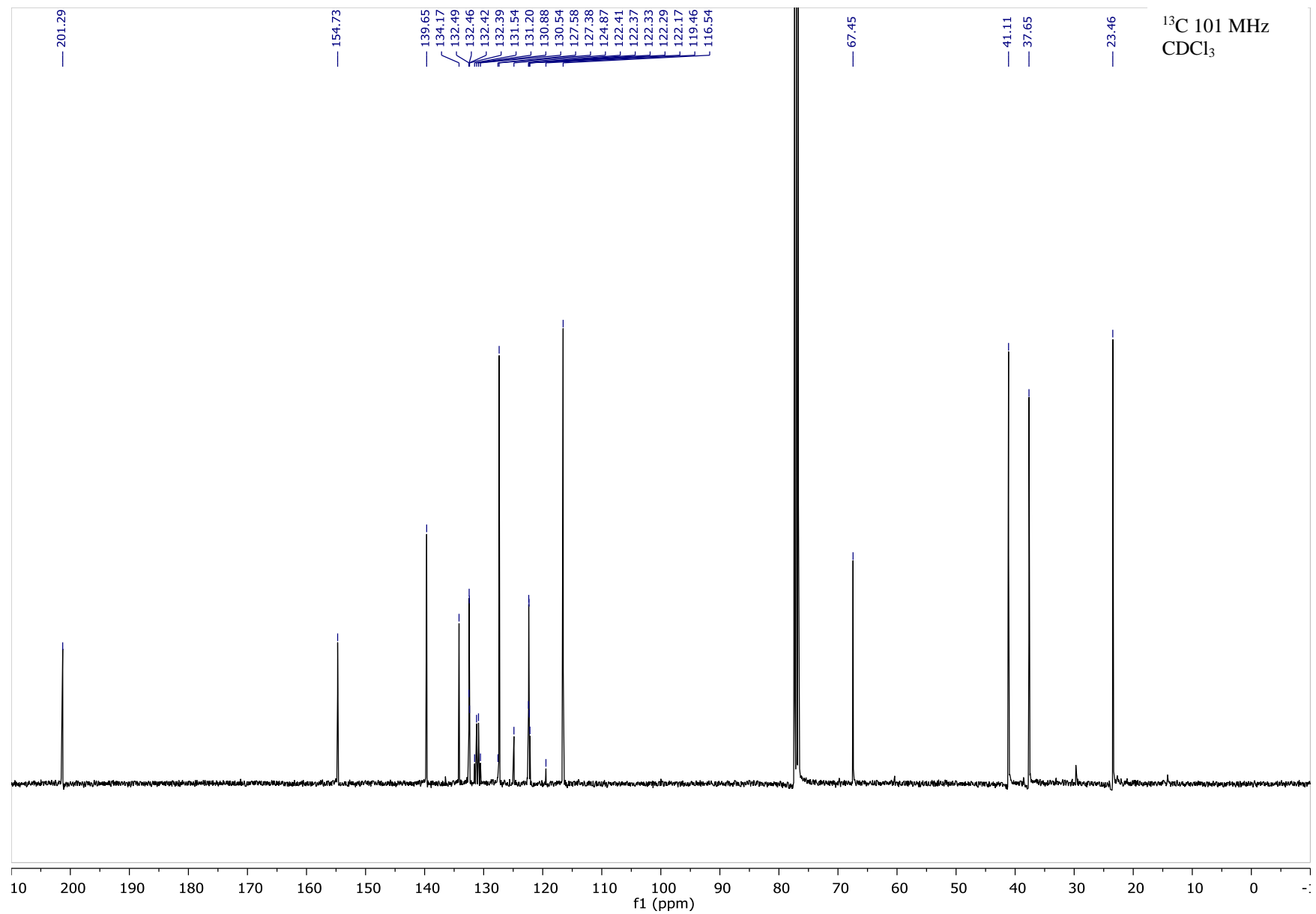


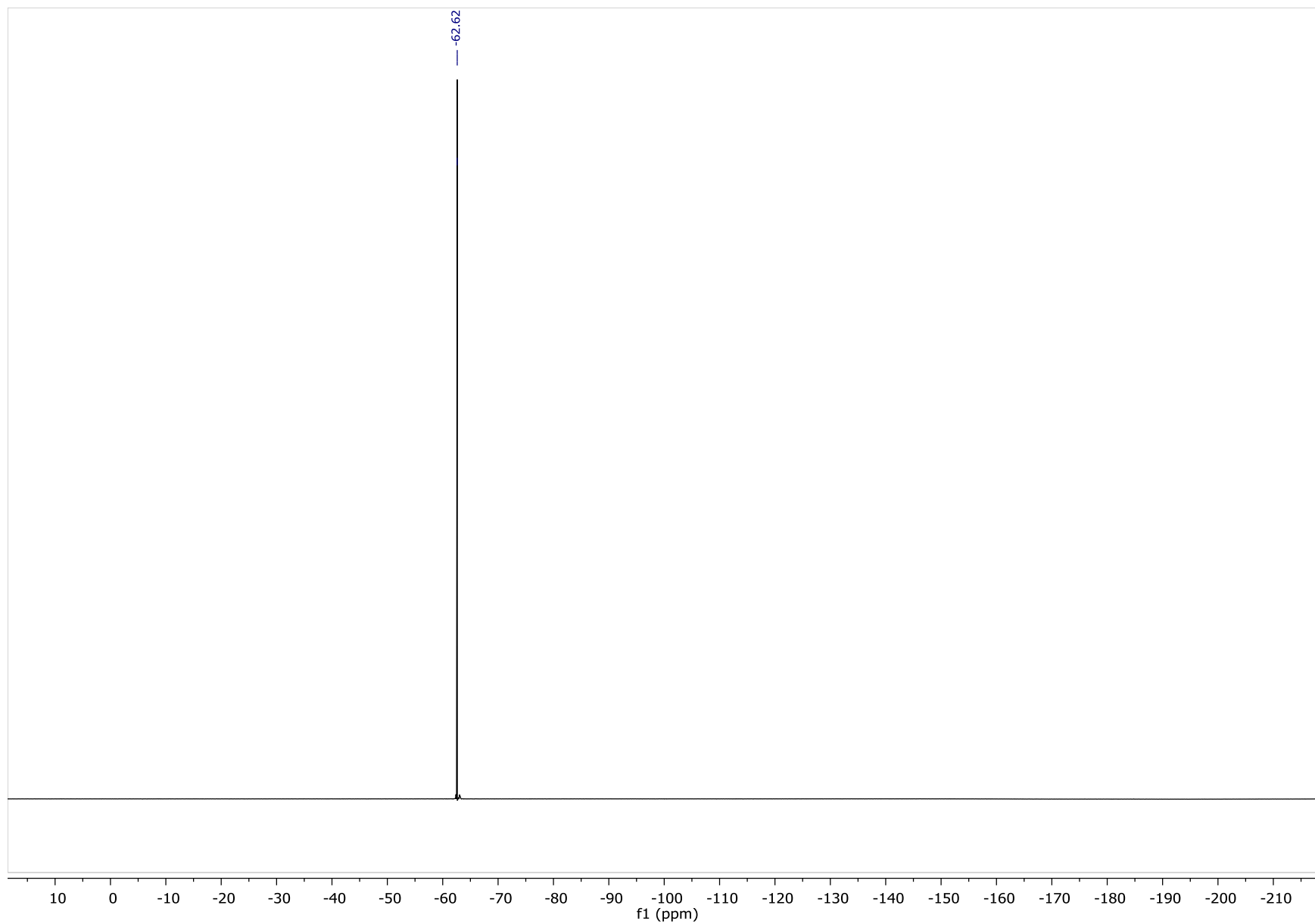
| # | Peak Name | CH | tR | Area | Height | Area% | Height% | Quantity | NTP | Resolution | Symmetry Factor | Warning |
|---|-----------|----|-------|---------|--------|--------|---------|----------|------|------------|-----------------|---------|
| 1 | Unknown | 1 | 6.413 | 234928 | 23885 | 6.501 | 8.945 | N/A | 9715 | 4.996 | 1.168 | |
| 2 | Unknown | 1 | 7.950 | 3378638 | 243143 | 93.499 | 91.055 | N/A | 7957 | N/A | 1.695 | |

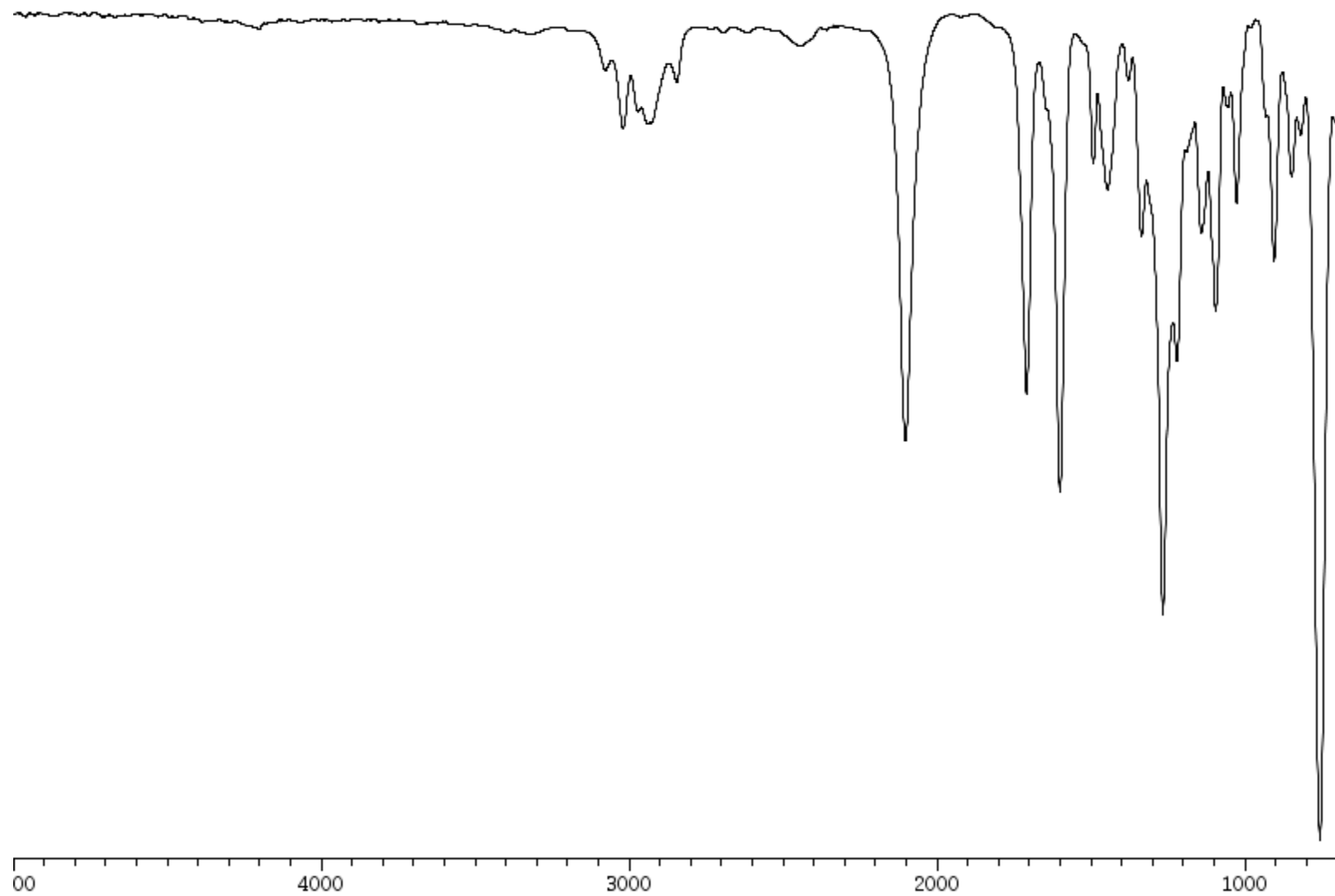


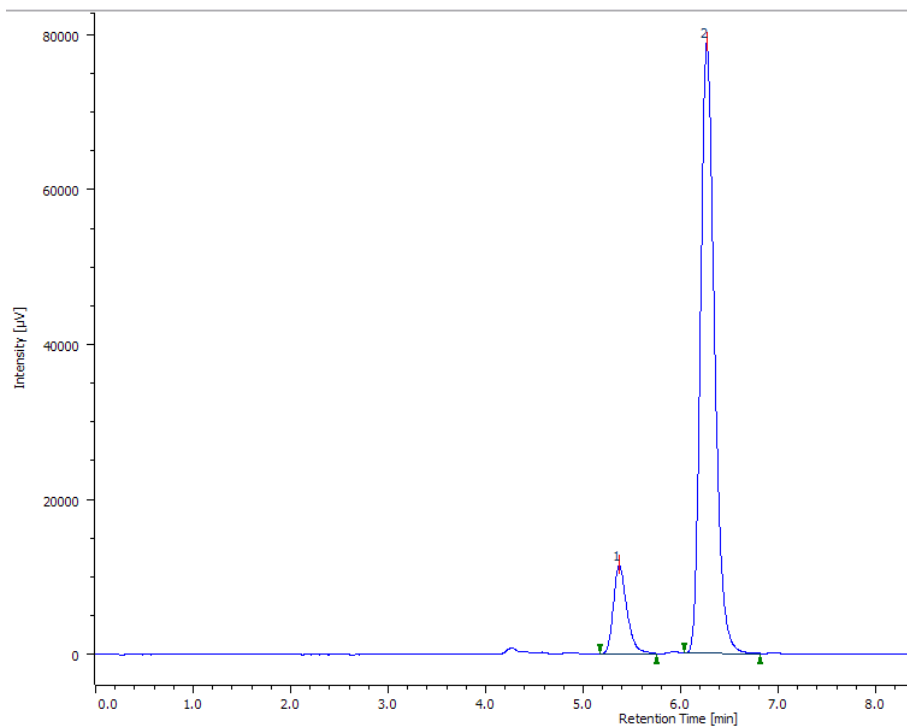
| # | Peak Name | CH | tR | Area | Height | Area% | Height% | Quantity | NTP | Resolution | Symmetry Factor | Warning |
|---|-----------|----|-------|---------|--------|--------|---------|----------|------|------------|-----------------|---------|
| 1 | Unknown | 1 | 6.400 | 3068988 | 234017 | 49.272 | 54.295 | N/A | 5349 | 4.052 | 1.103 | |
| 2 | Unknown | 1 | 7.947 | 3159714 | 196993 | 60.728 | 45.705 | N/A | 5856 | N/A | 1.479 | |



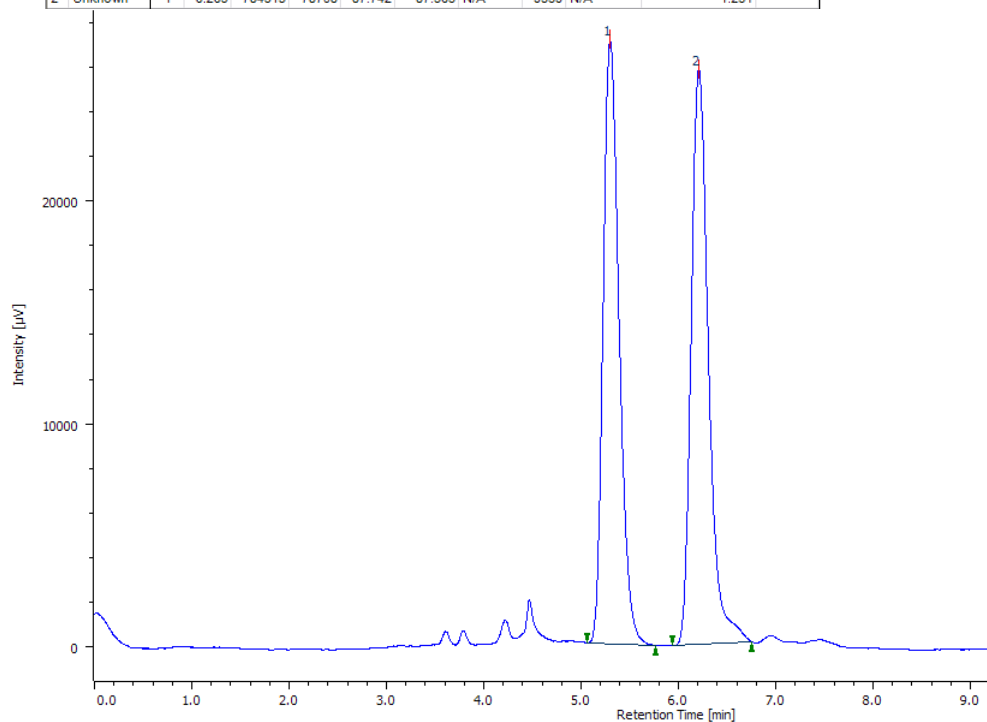




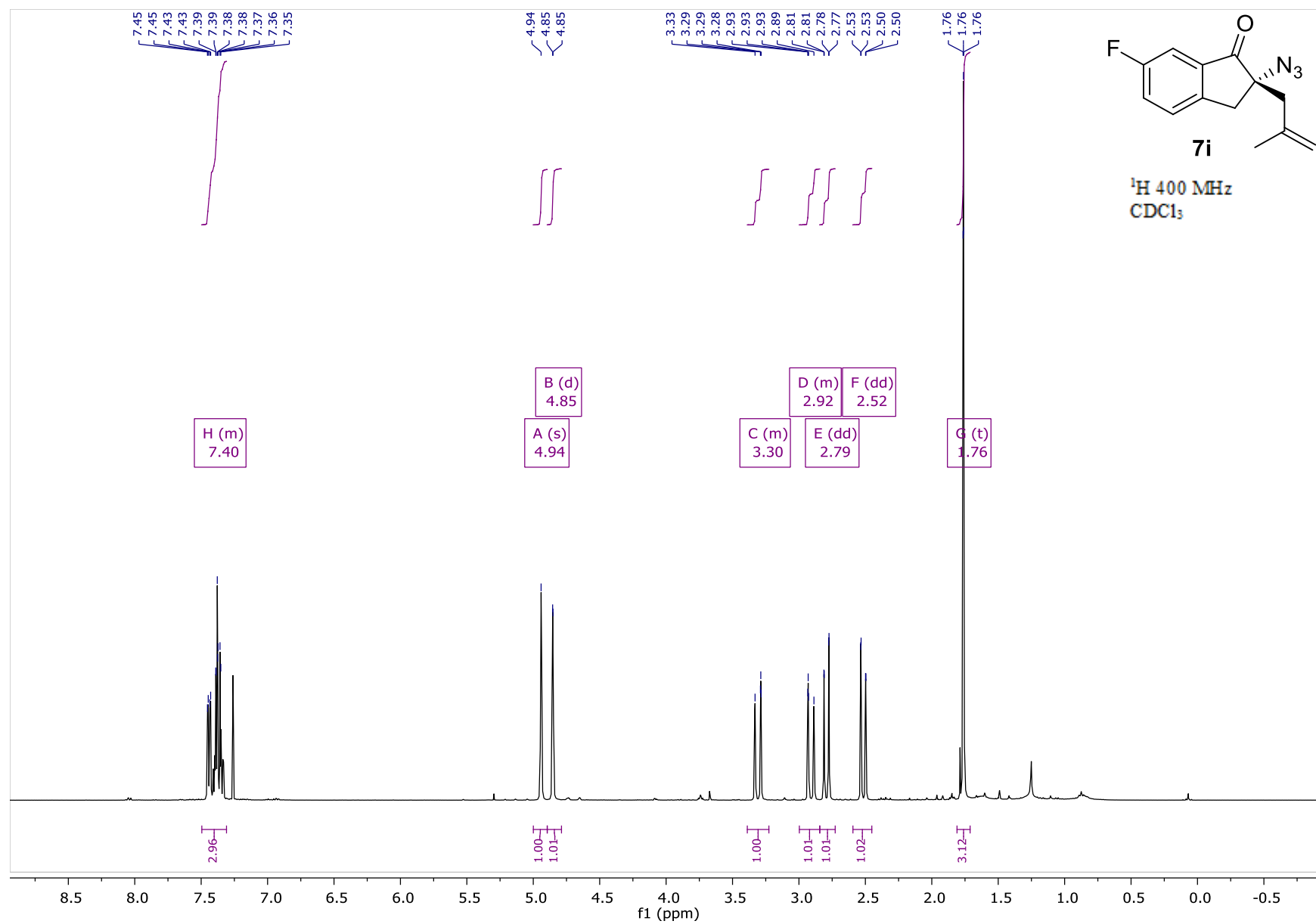


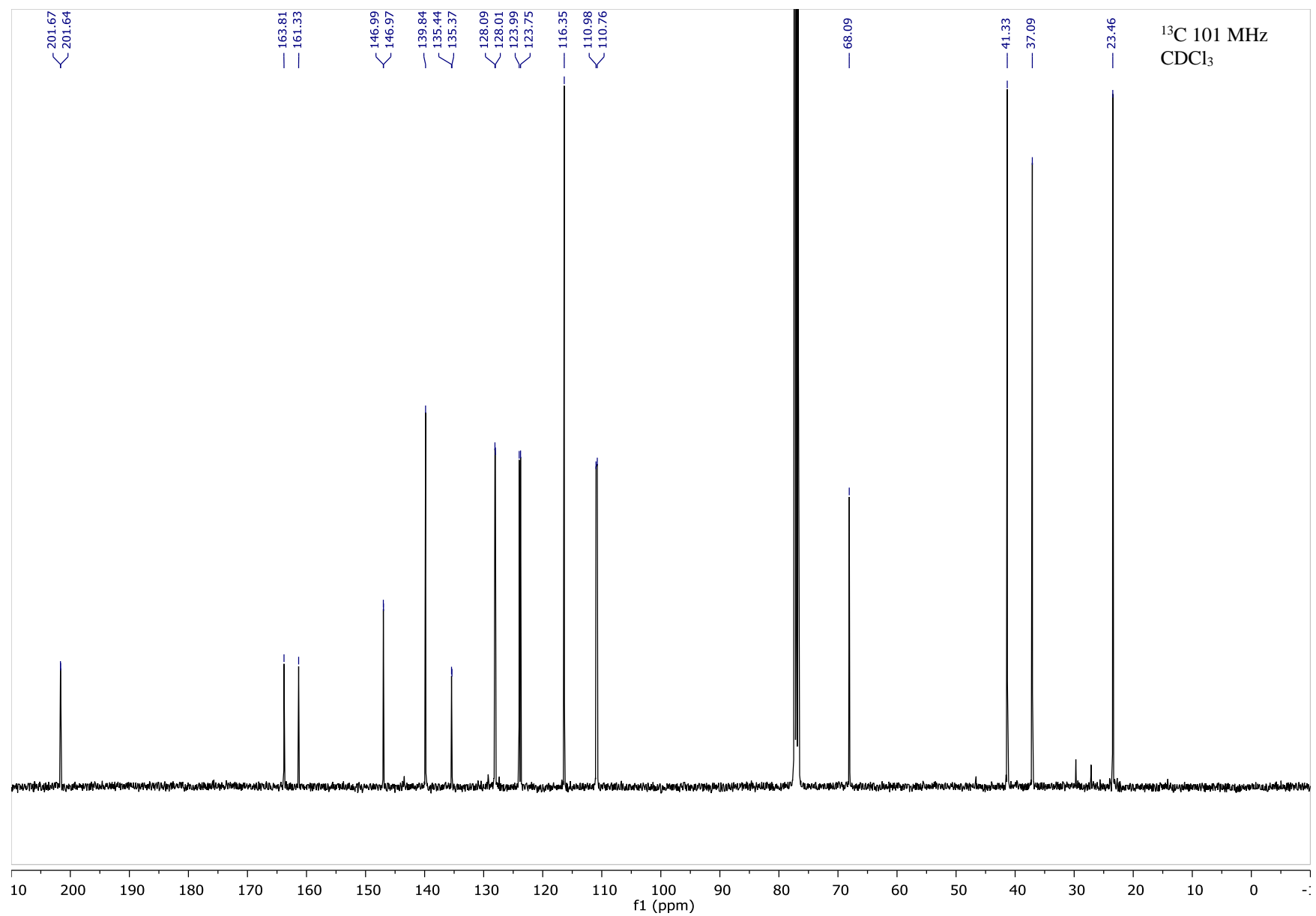


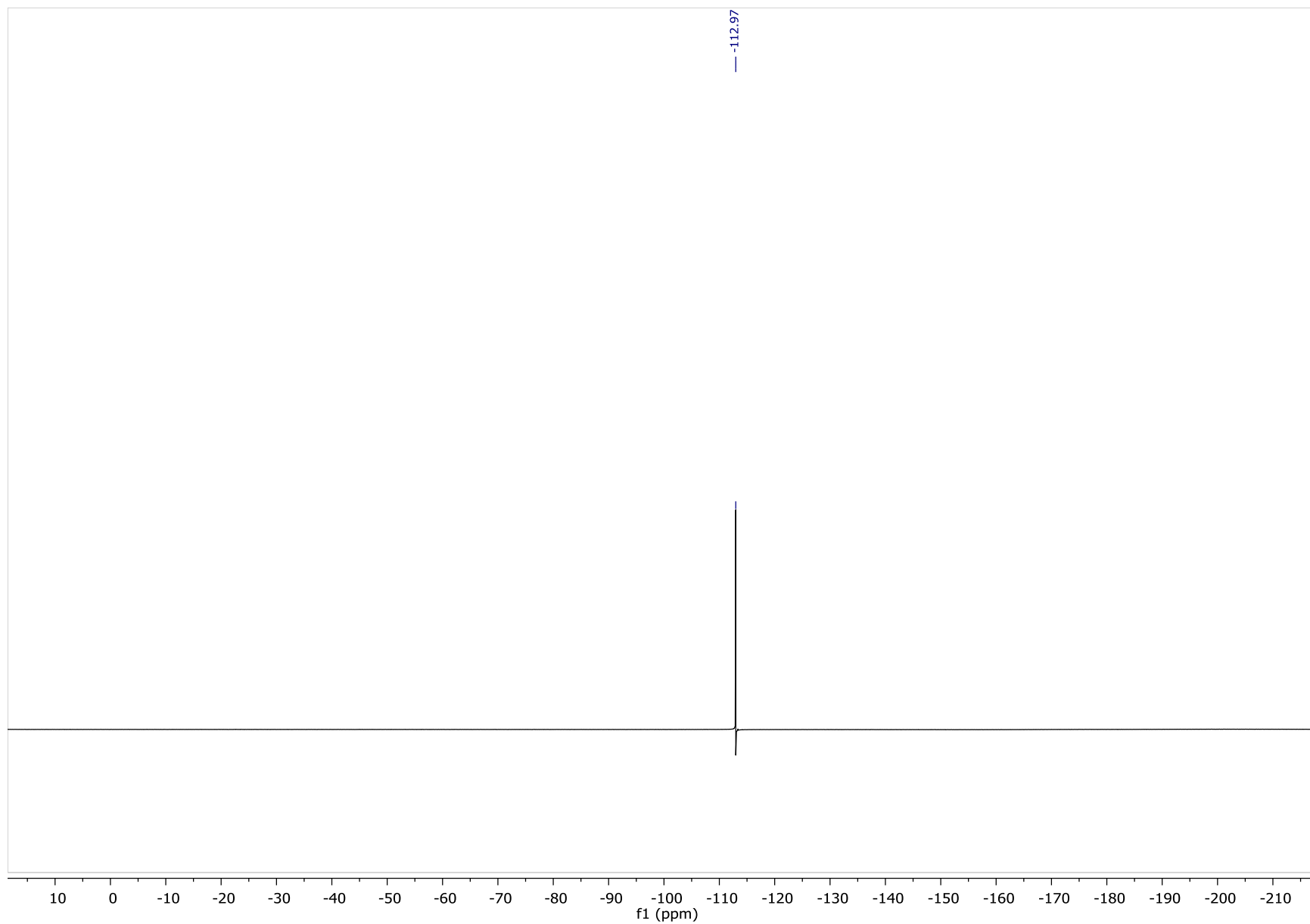
| # | Peak Name | CH | tR | Area | Height | Area% | Height% | Quantity | NTP | Resolution | Symmetry Factor | Warning |
|---|-----------|----|-------|--------|--------|--------|---------|----------|------|------------|-----------------|---------|
| 1 | Unknown | 1 | 5.363 | 109570 | 11385 | 12.258 | 12.637 | N/A | 7694 | 3.602 | 1.333 | |
| 2 | Unknown | 1 | 6.263 | 784315 | 78708 | 87.742 | 87.363 | N/A | 9539 | N/A | 1.231 | |

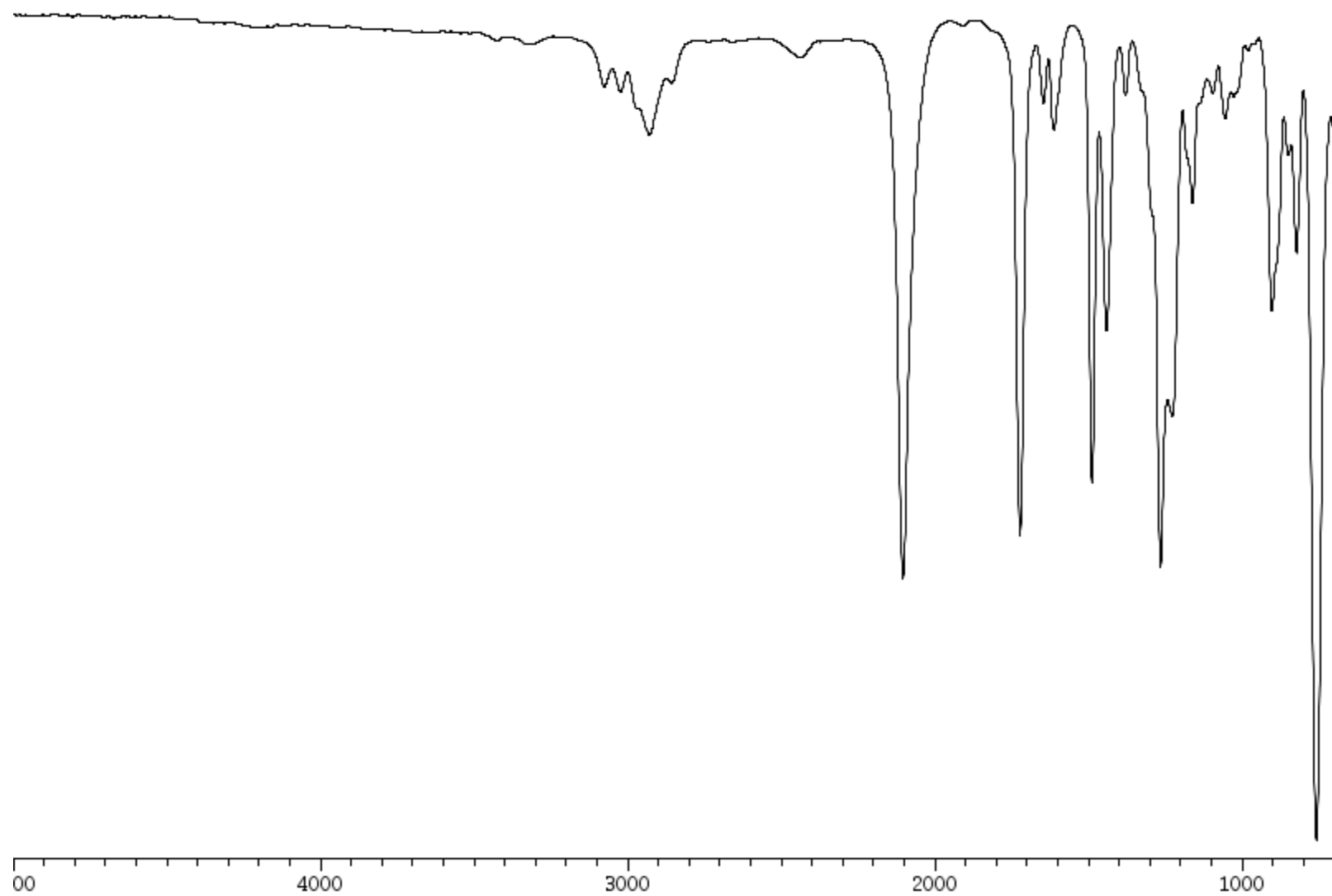


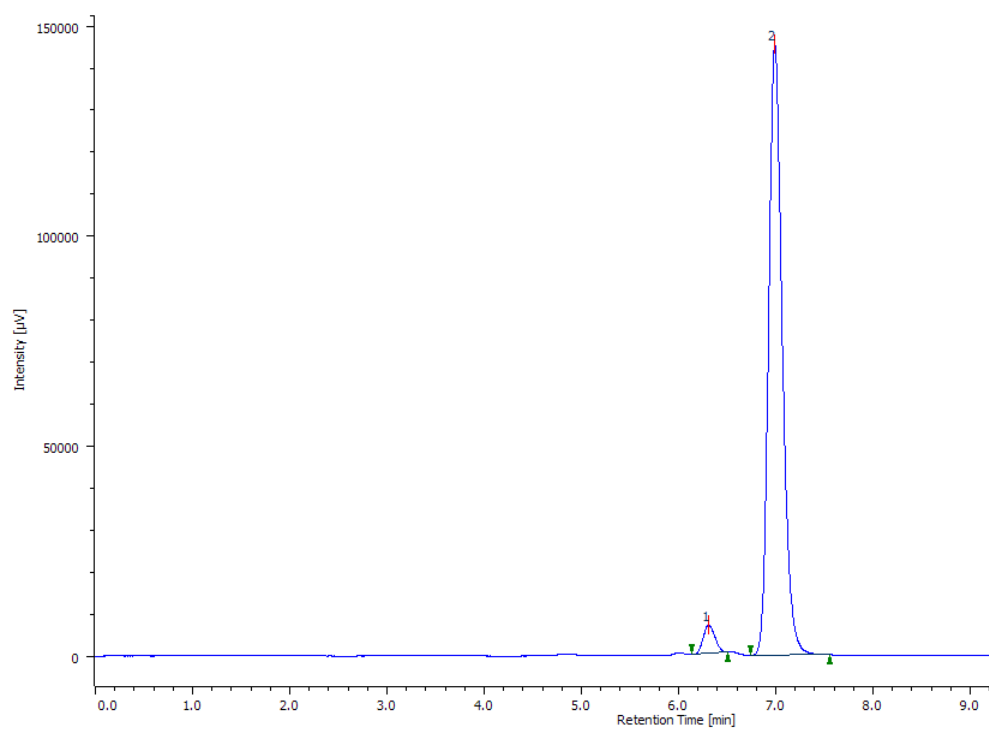
| # | Peak Name | CH | tR | Area | Height | Area% | Height% | Quantity | NTP | Resolution | Symmetry Factor | Warning |
|---|-----------|----|-------|--------|--------|--------|---------|----------|------|------------|-----------------|---------|
| 1 | Unknown | 1 | 5.293 | 308061 | 27049 | 49.170 | 51.191 | N/A | 5026 | 2.986 | 1.276 | |
| 2 | Unknown | 1 | 6.203 | 318462 | 25790 | 50.830 | 48.809 | N/A | 6307 | N/A | 1.327 | |



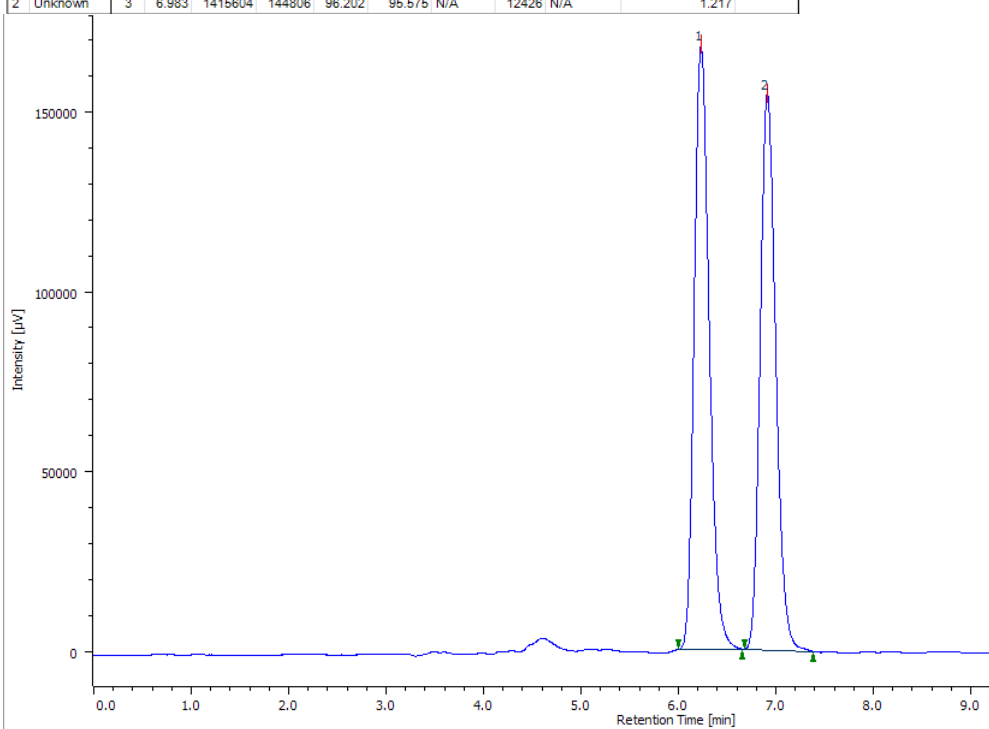




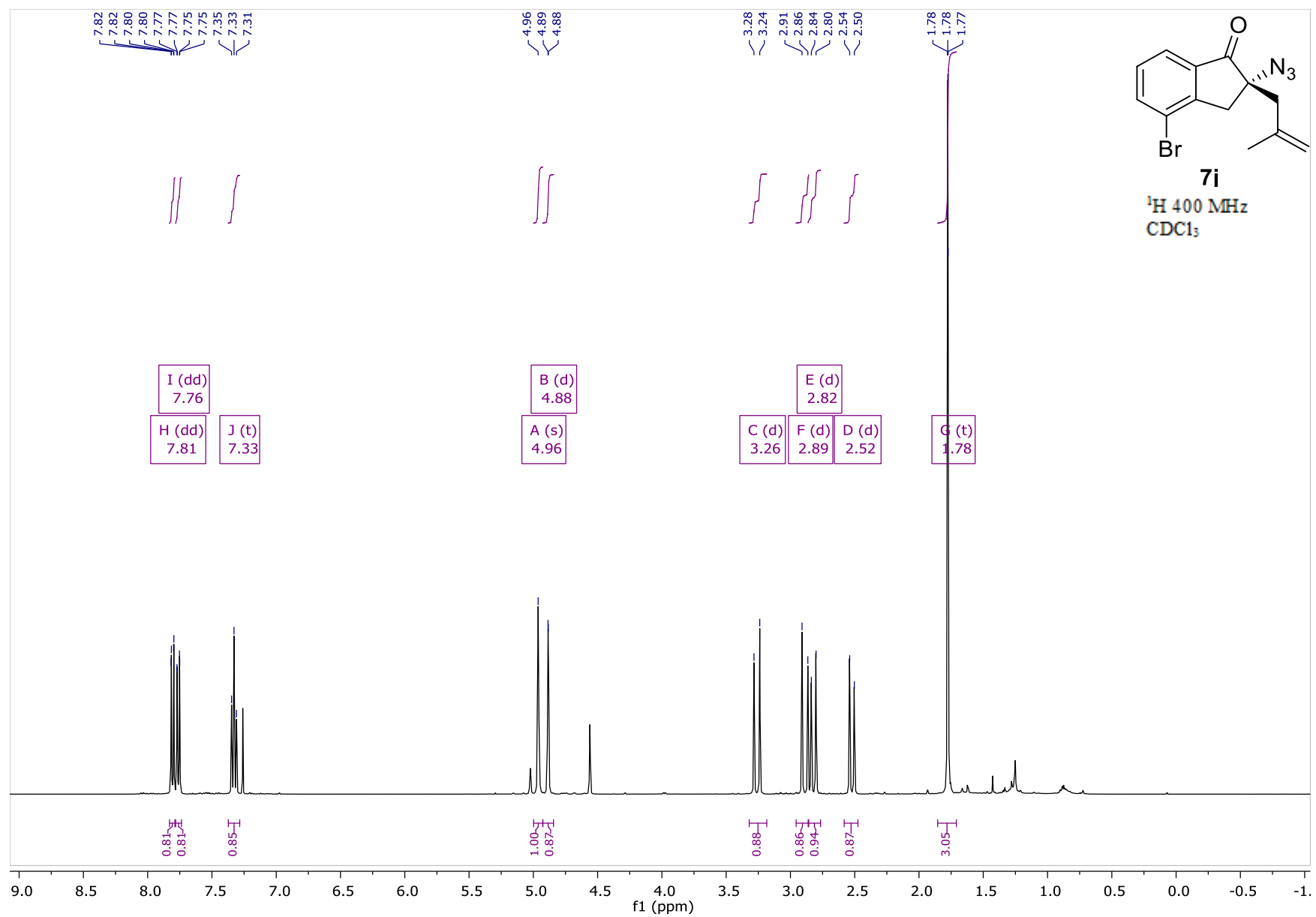


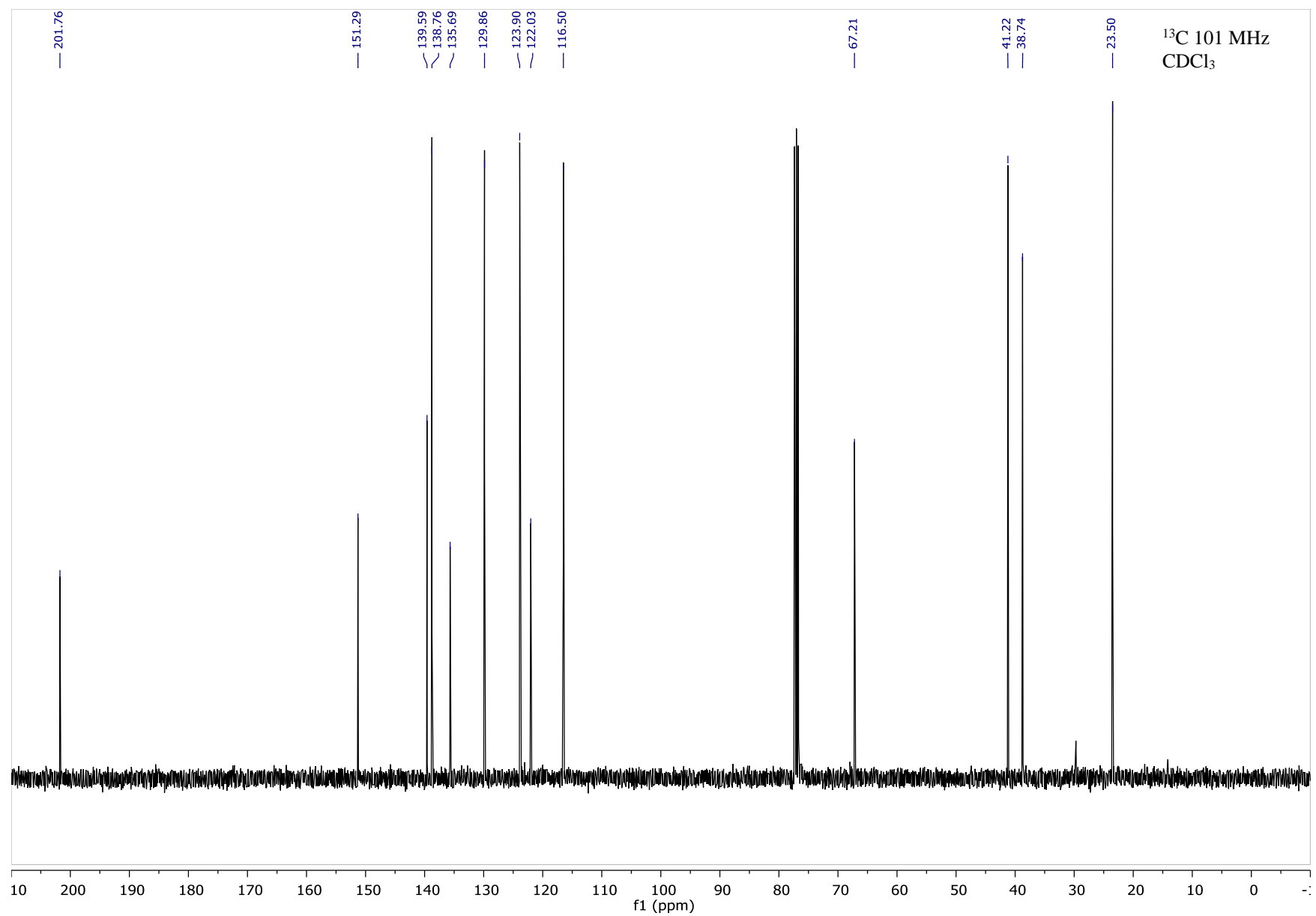


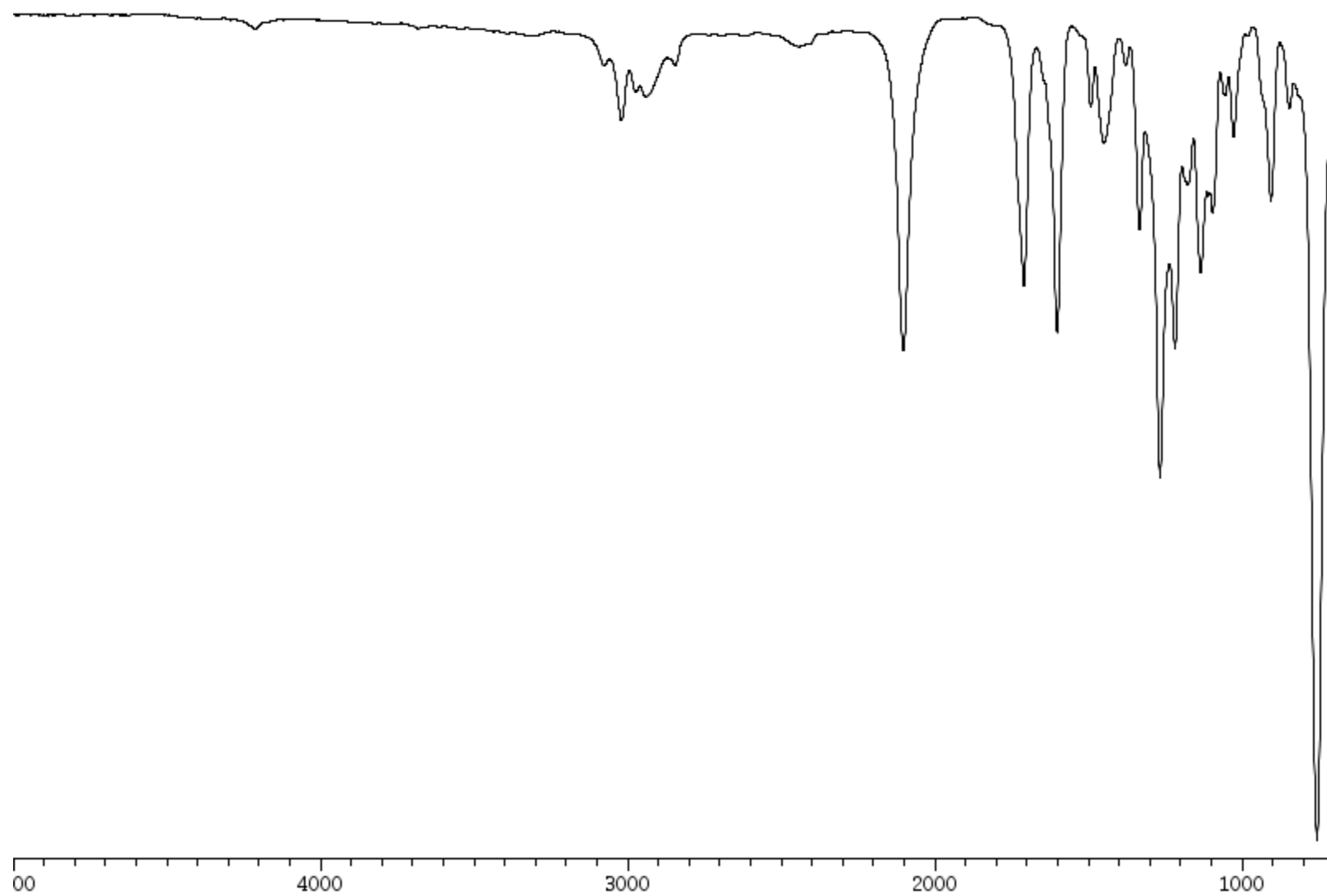
| # | Peak Name | CH | tR | Area | Height | Area% | Height% | Quantity | NTP | Resolution | Symmetry Factor | Warning |
|---|-----------|----|-------|---------|--------|--------|---------|----------|-------|------------|-----------------|---------|
| 1 | Unknown | 3 | 6.303 | 55885 | 6704 | 3.798 | 4.425 | N/A | 12583 | 2.869 | 1.106 | |
| 2 | Unknown | 3 | 6.983 | 1415604 | 144806 | 96.202 | 95.575 | N/A | 12426 | N/A | 1.217 | |

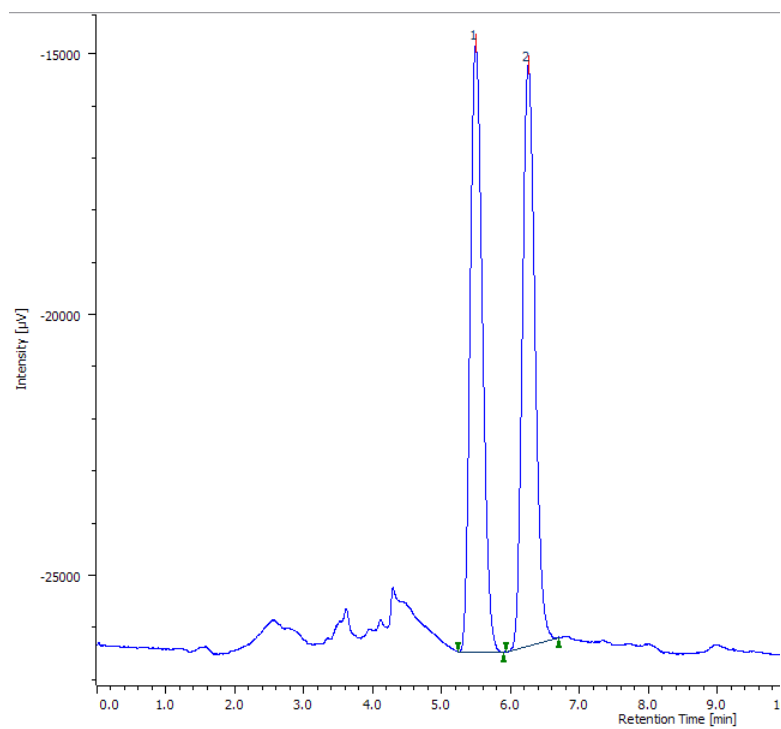


| # | Peak Name | CH | tR | Area | Height | Area% | Height% | Quantity | NTP | Resolution | Symmetry Factor | Warning |
|---|-----------|----|-------|---------|--------|--------|---------|----------|------|------------|-----------------|---------|
| 1 | Unknown | 3 | 6.227 | 1800690 | 167642 | 51.226 | 52.075 | N/A | 7935 | 2.392 | 1.217 | |
| 2 | Unknown | 3 | 6.907 | 1714464 | 154280 | 48.774 | 47.925 | N/A | 9050 | N/A | 1.178 | |

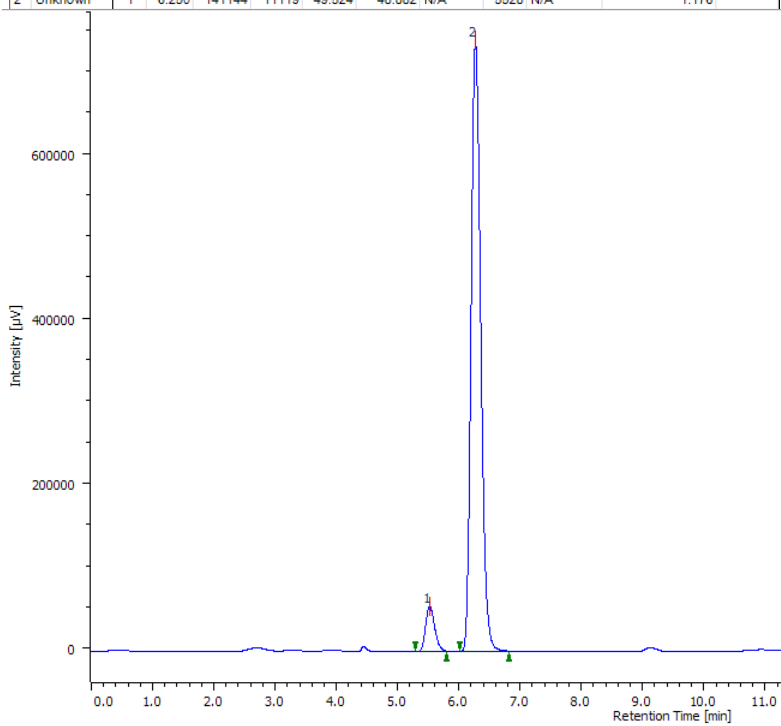




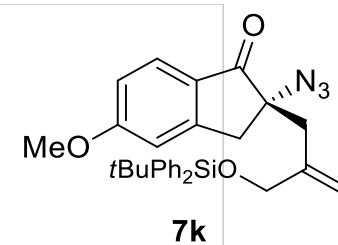




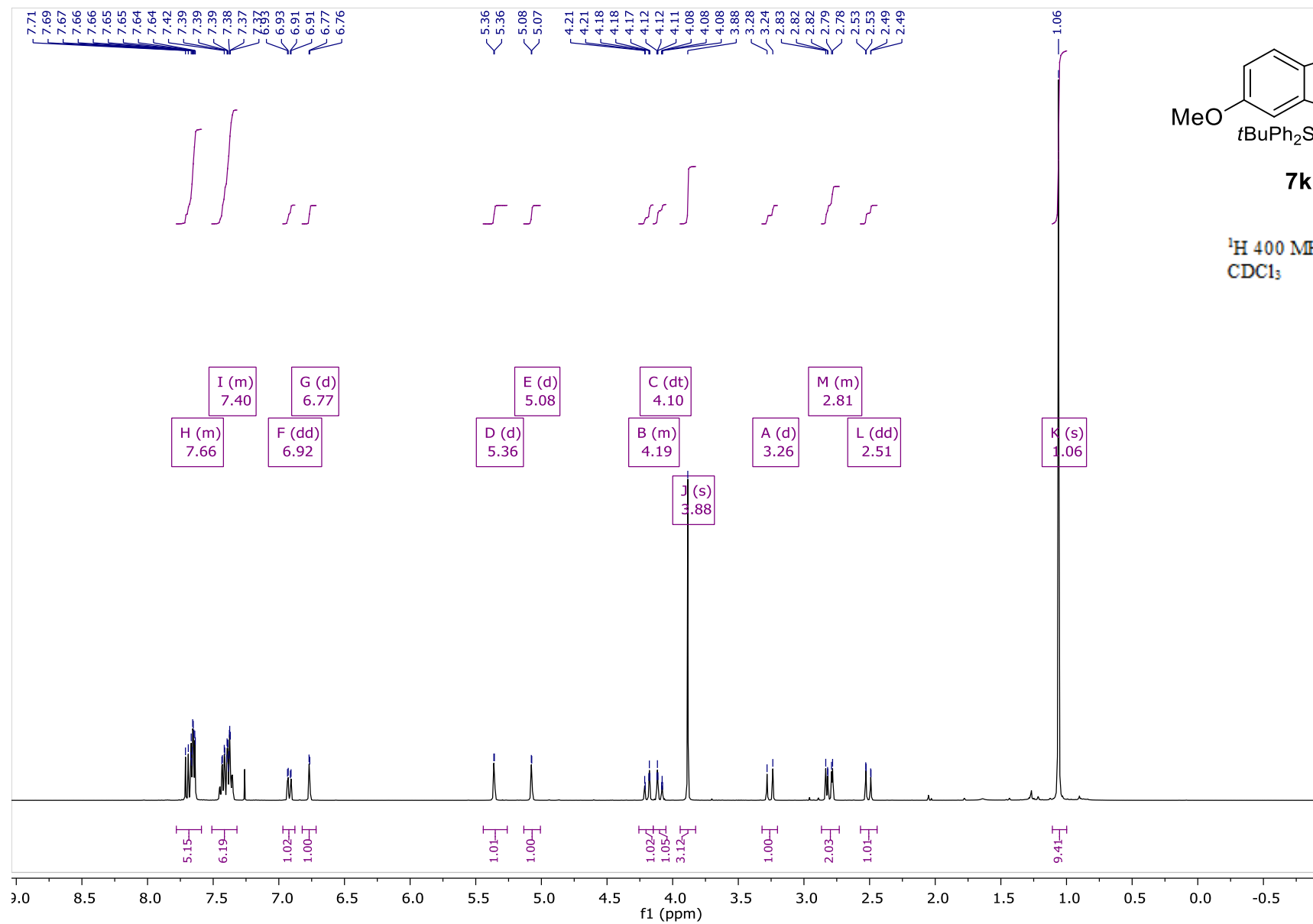
| # | Peak Name | CH | tR | Area | Height | Area% | Height% | Quantity | NTP | Resolution | Symmetry Factor | Warning |
|---|-----------|----|-------|--------|--------|--------|---------|----------|------|------------|-----------------|---------|
| 1 | Unknown | 1 | 5.490 | 143854 | 11627 | 50.476 | 51.118 | N/A | 4410 | 2.285 | 1.193 | |
| 2 | Unknown | 1 | 6.250 | 141144 | 11119 | 49.524 | 48.882 | N/A | 5528 | N/A | 1.176 | |

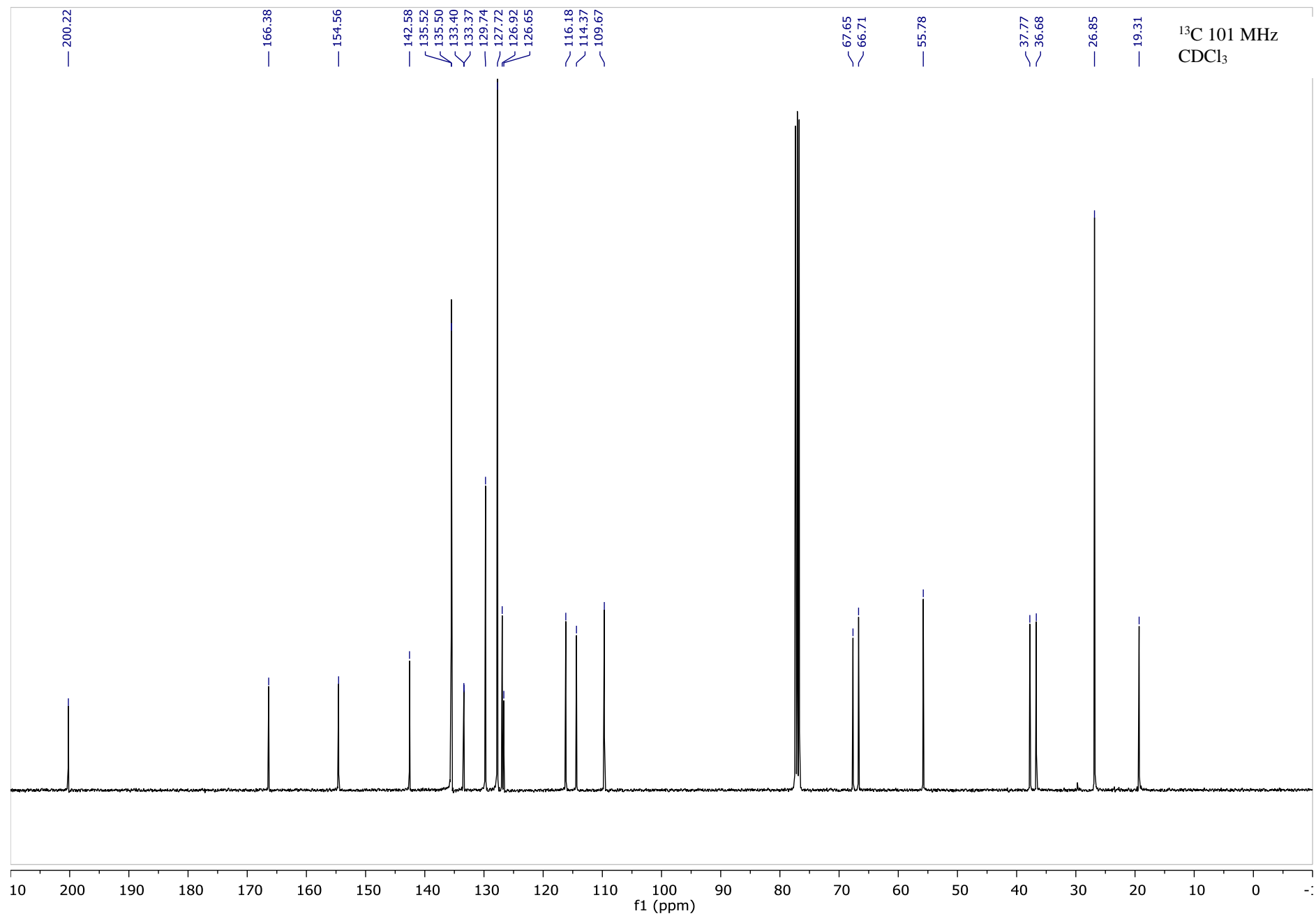


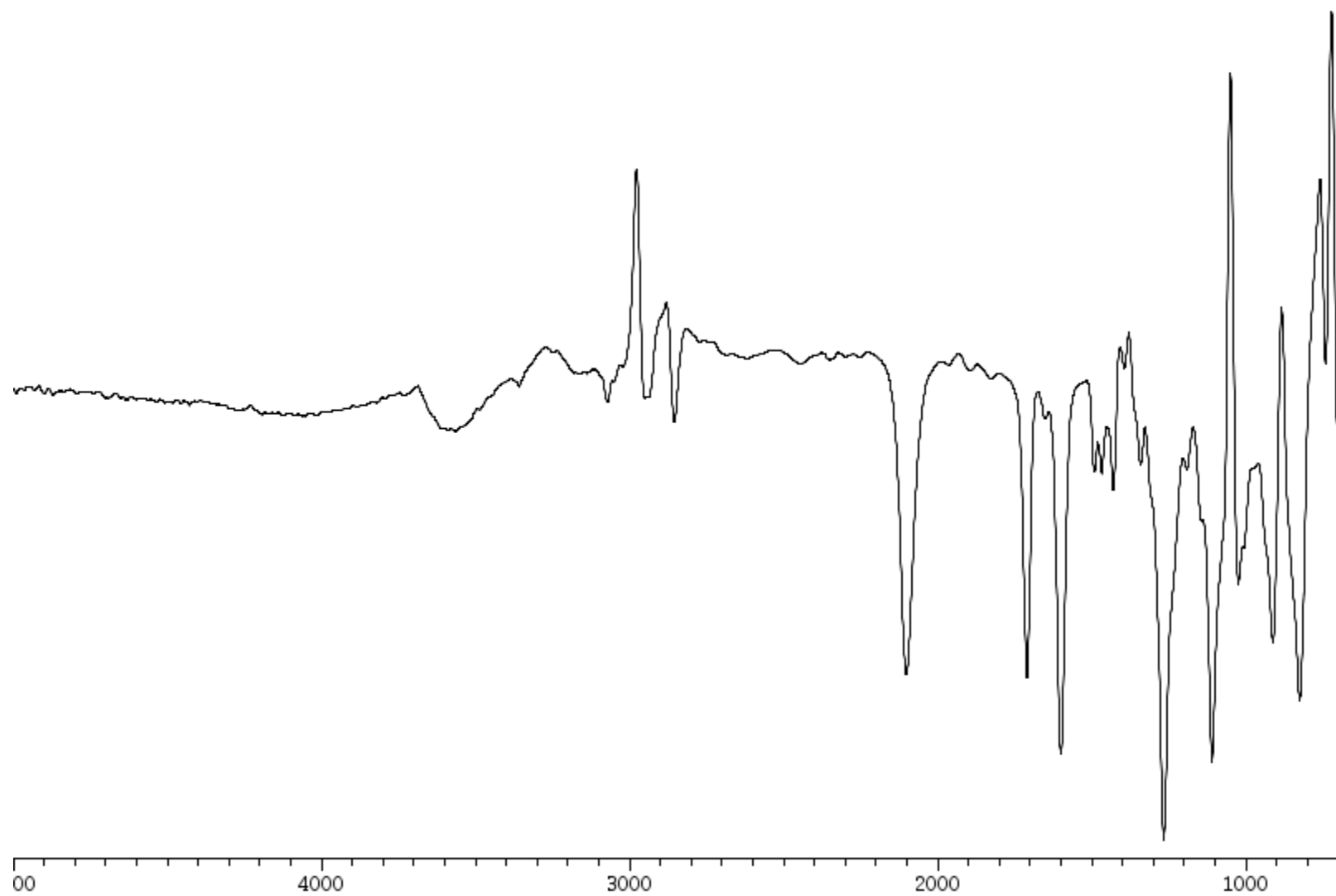
| # | Peak Name | CH | tR | Area | Height | Area% | Height% | Quantity | NTP | Resolution | Symmetry Factor | Warning |
|---|-----------|----|-------|---------|--------|--------|---------|----------|------|------------|-----------------|---------|
| 1 | Unknown | 1 | 5.517 | 563966 | 54616 | 6.531 | 6.886 | N/A | 6574 | 2.689 | 1.221 | |
| 2 | Unknown | 1 | 6.267 | 8071280 | 738555 | 93.469 | 93.114 | N/A | 7625 | N/A | 1.198 | |

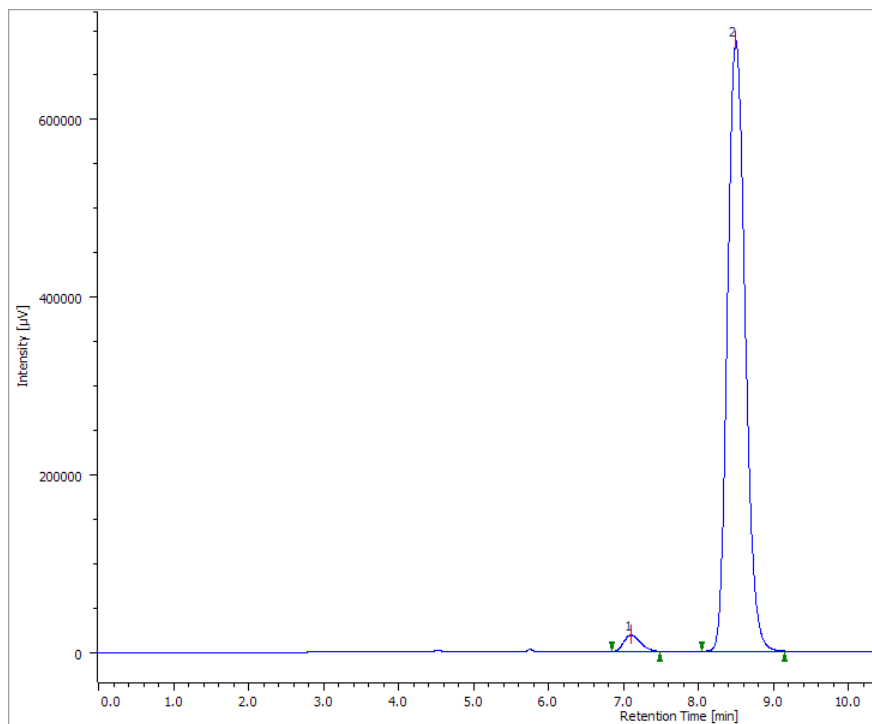


¹H 400 MHz
 CDCl₃

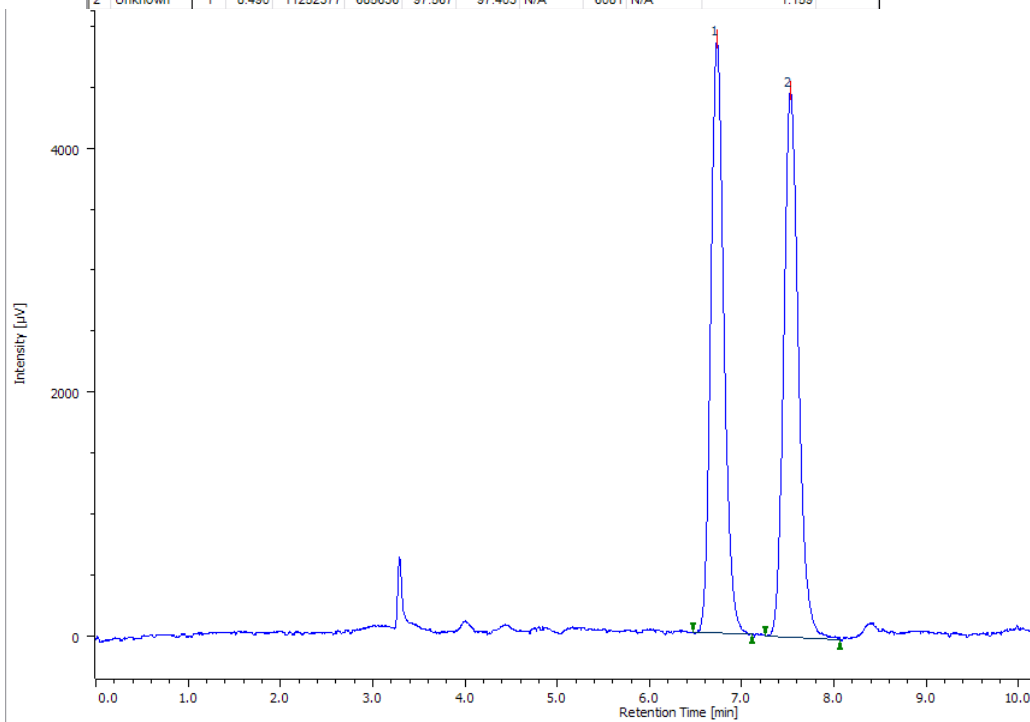




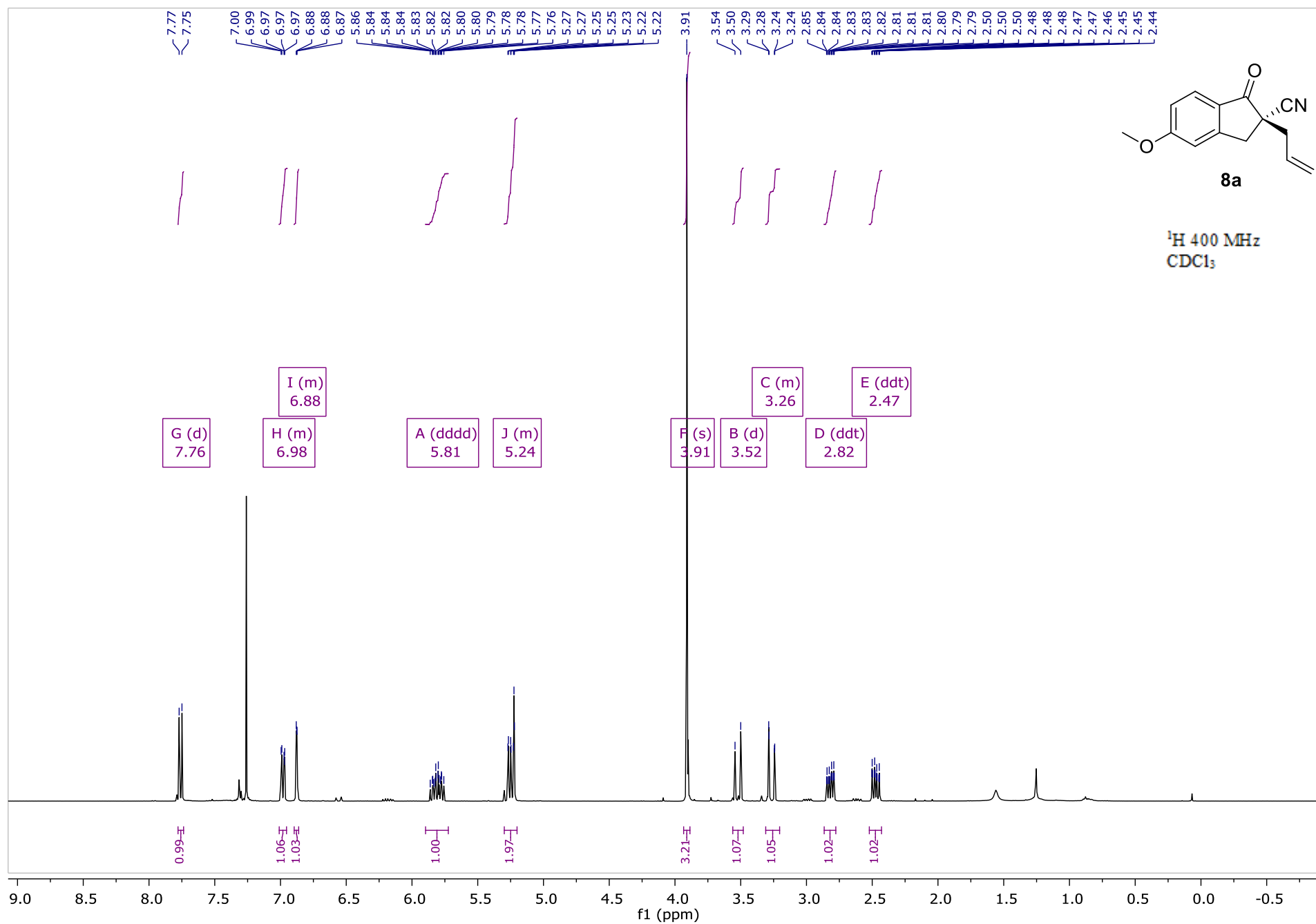


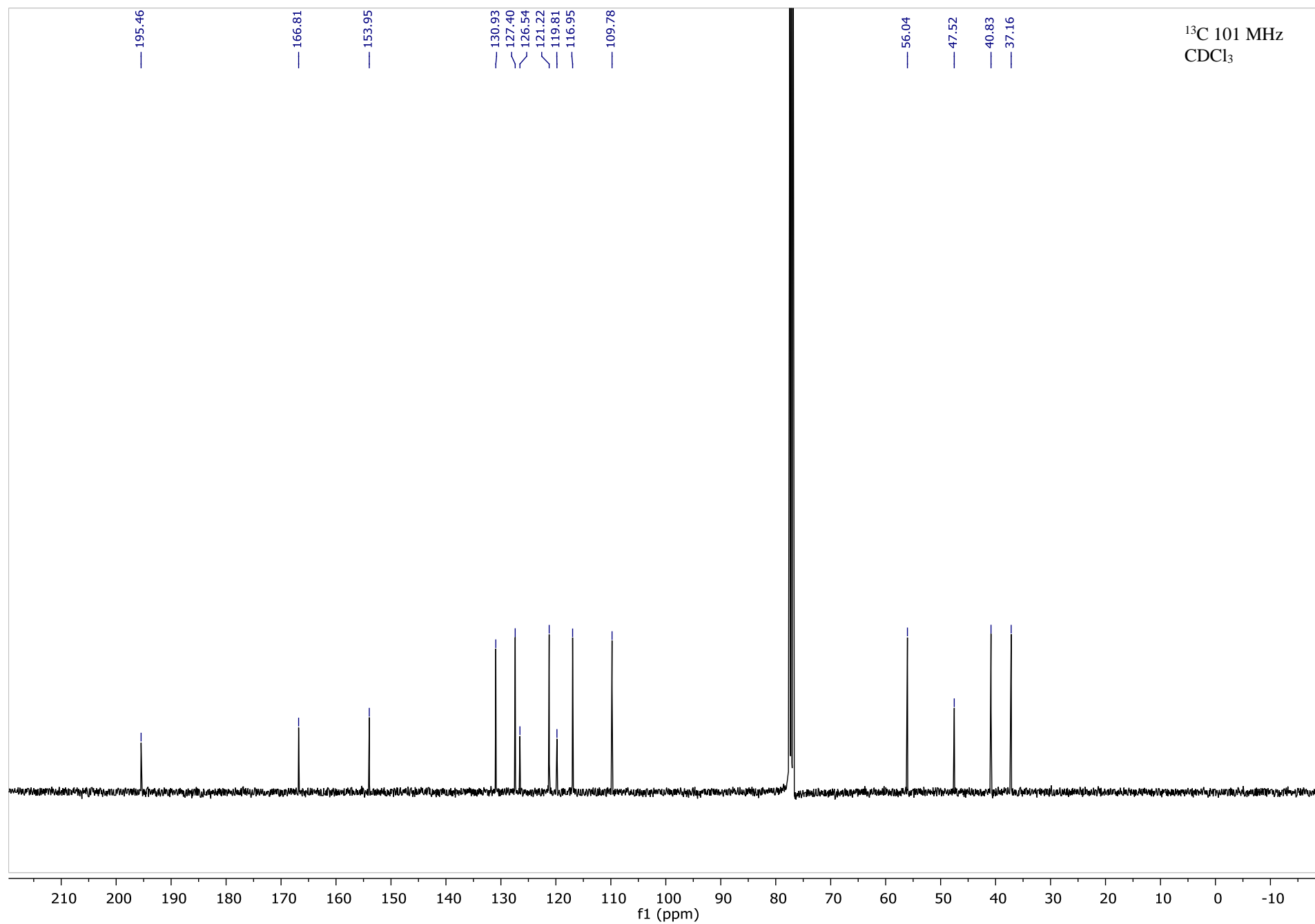


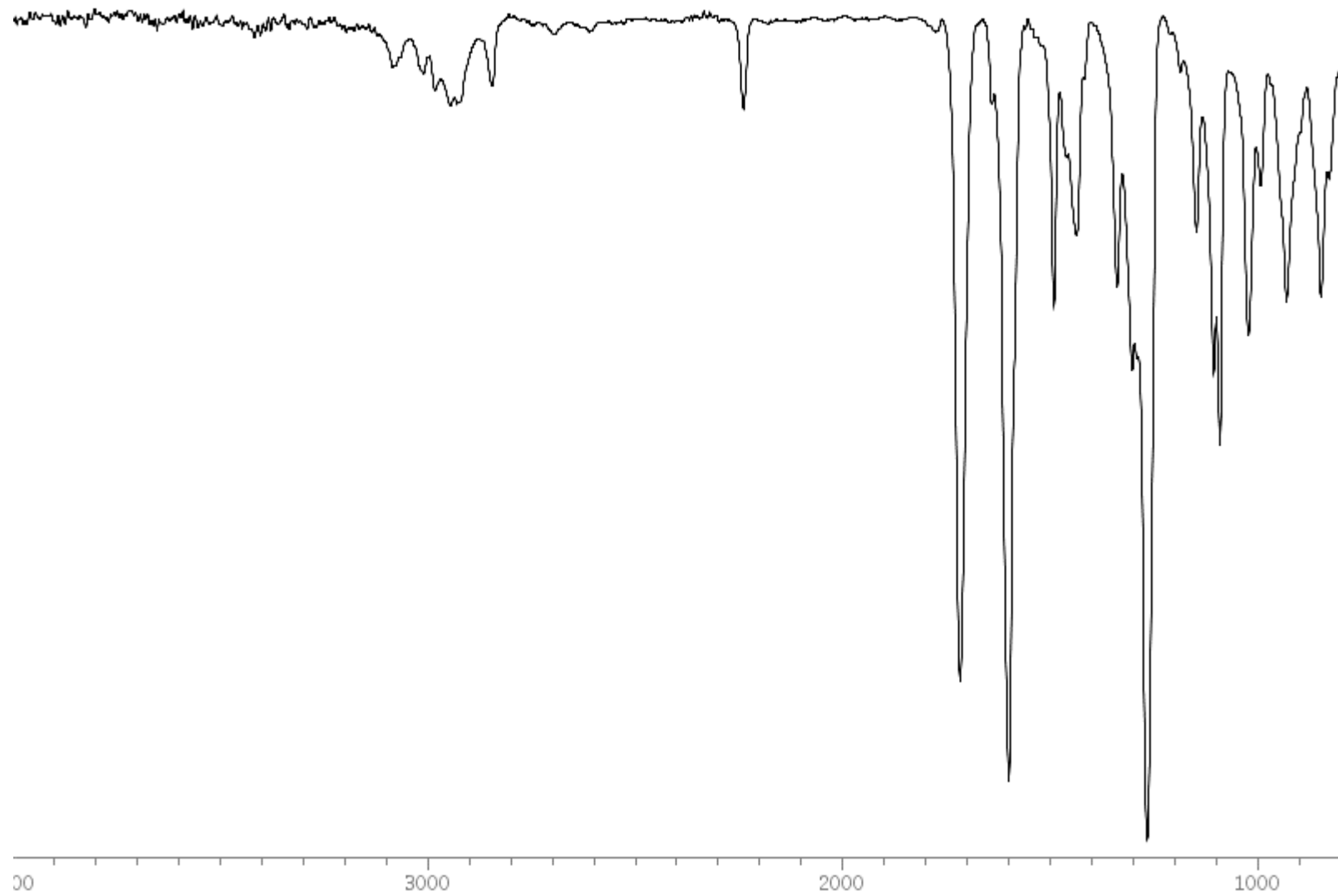
| # | Peak Name | CH | tR | Area | Height | Area% | Height% | Quantity | NTP | Resolution | Symmetry Factor | Warning |
|---|-----------|----|-------|----------|--------|--------|---------|----------|------|------------|-----------------|---------|
| 1 | Unknown | 1 | 7.093 | 280639 | 18283 | 2.433 | 2.597 | N/A | 4881 | 3.328 | 1.294 | |
| 2 | Unknown | 1 | 8.490 | 11252377 | 685636 | 97.567 | 97.403 | N/A | 6081 | N/A | 1.159 | |

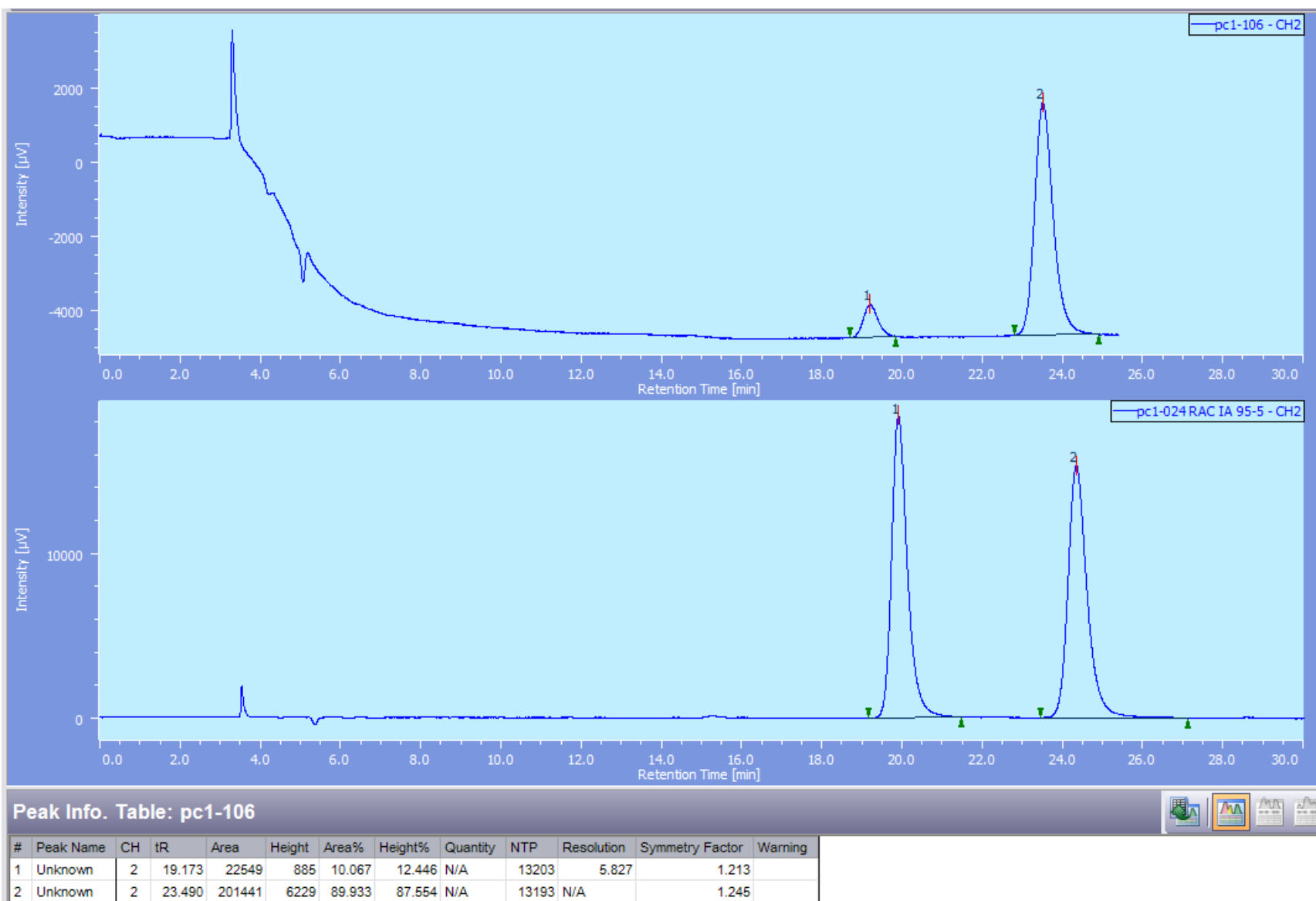


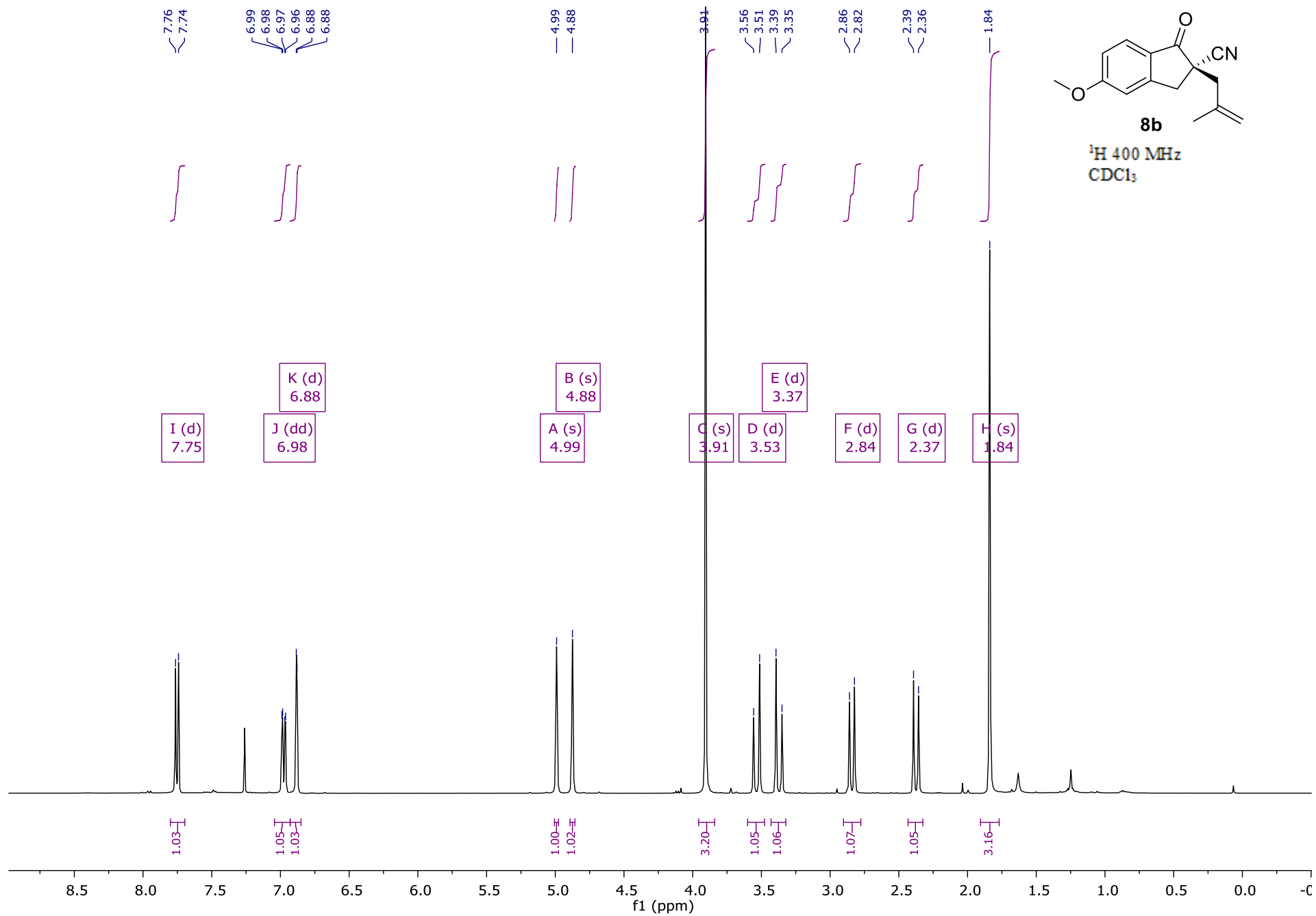
| # | Peak Name | CH | tR | Area | Height | Area% | Height% | Quantity | NTP | Resolution | Symmetry Factor | Warning |
|---|-----------|----|-------|-------|--------|--------|---------|----------|-------|------------|-----------------|---------|
| 1 | Unknown | 1 | 6.723 | 48058 | 4861 | 49.316 | 52.106 | N/A | 11032 | 2.956 | 1.169 | |
| 2 | Unknown | 1 | 7.620 | 49391 | 4468 | 50.684 | 47.894 | N/A | 11184 | N/A | 1.187 | |

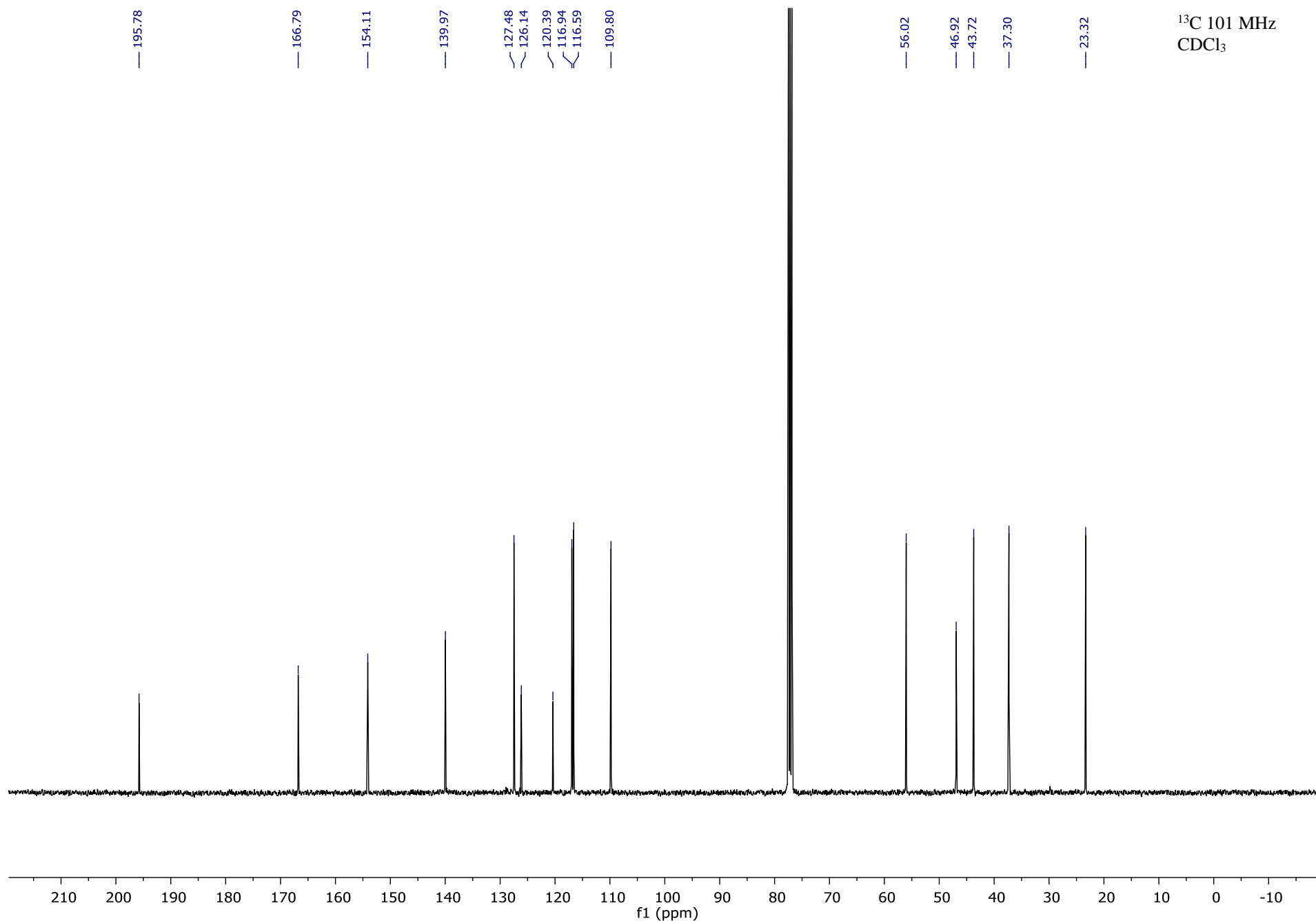


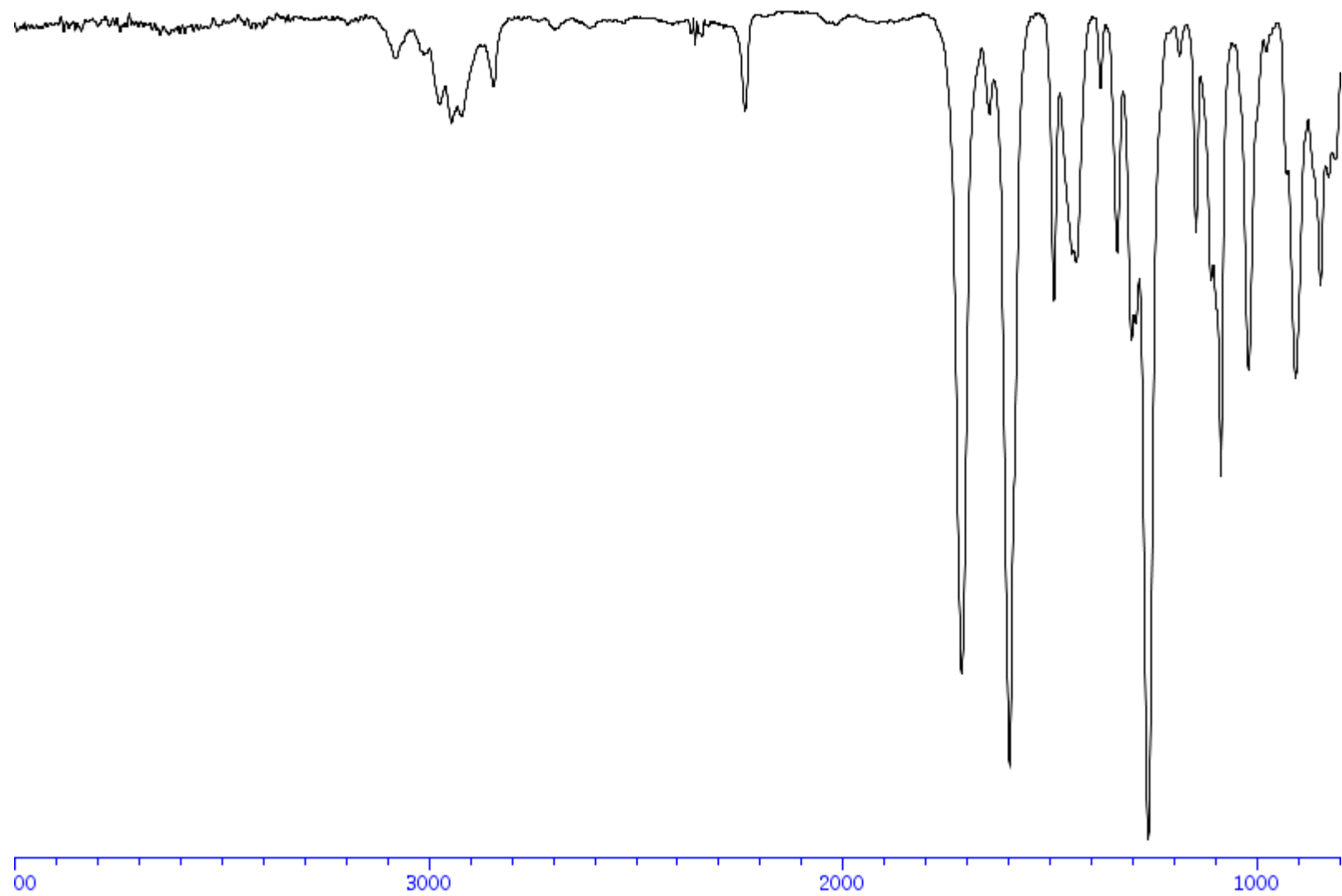


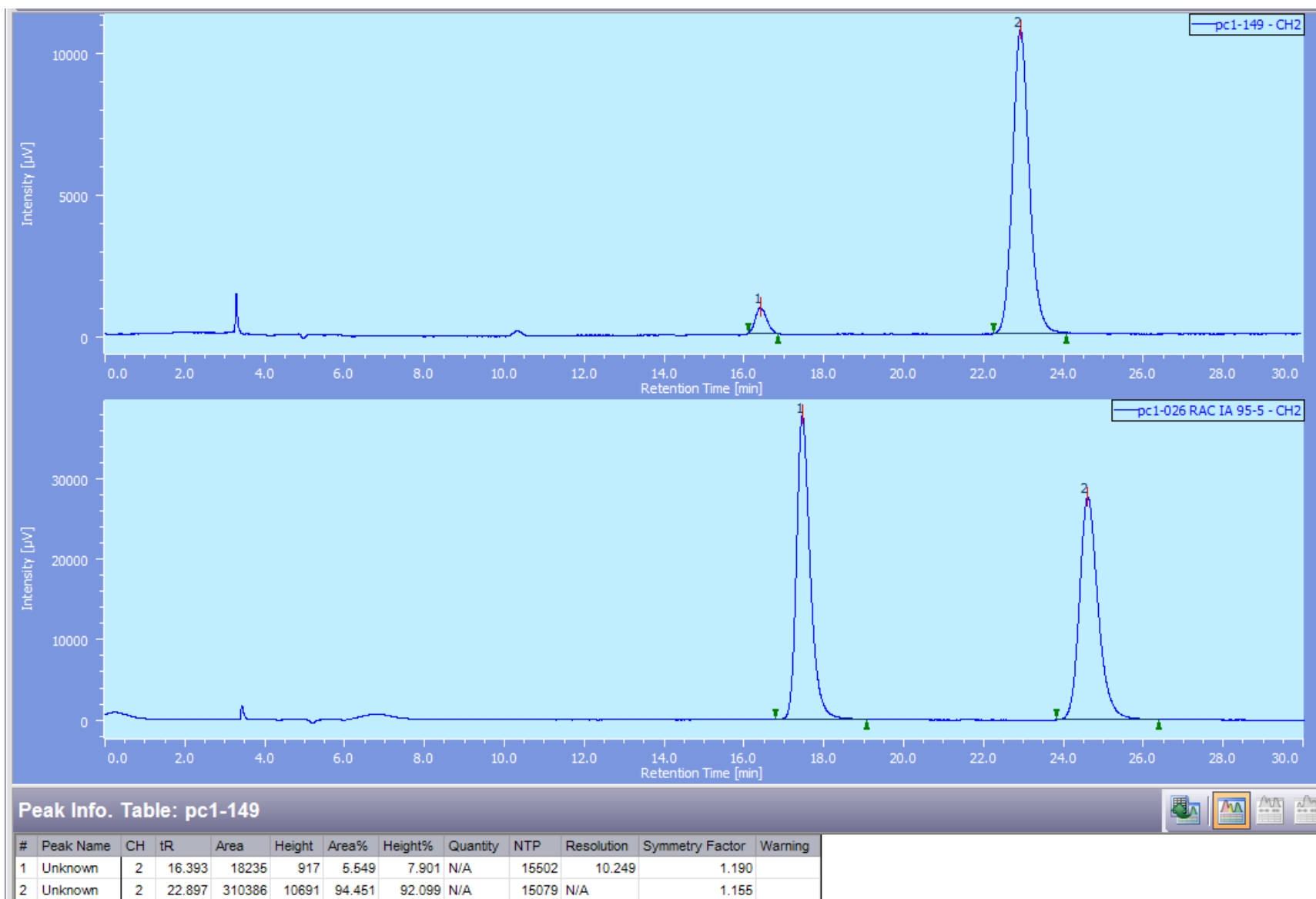


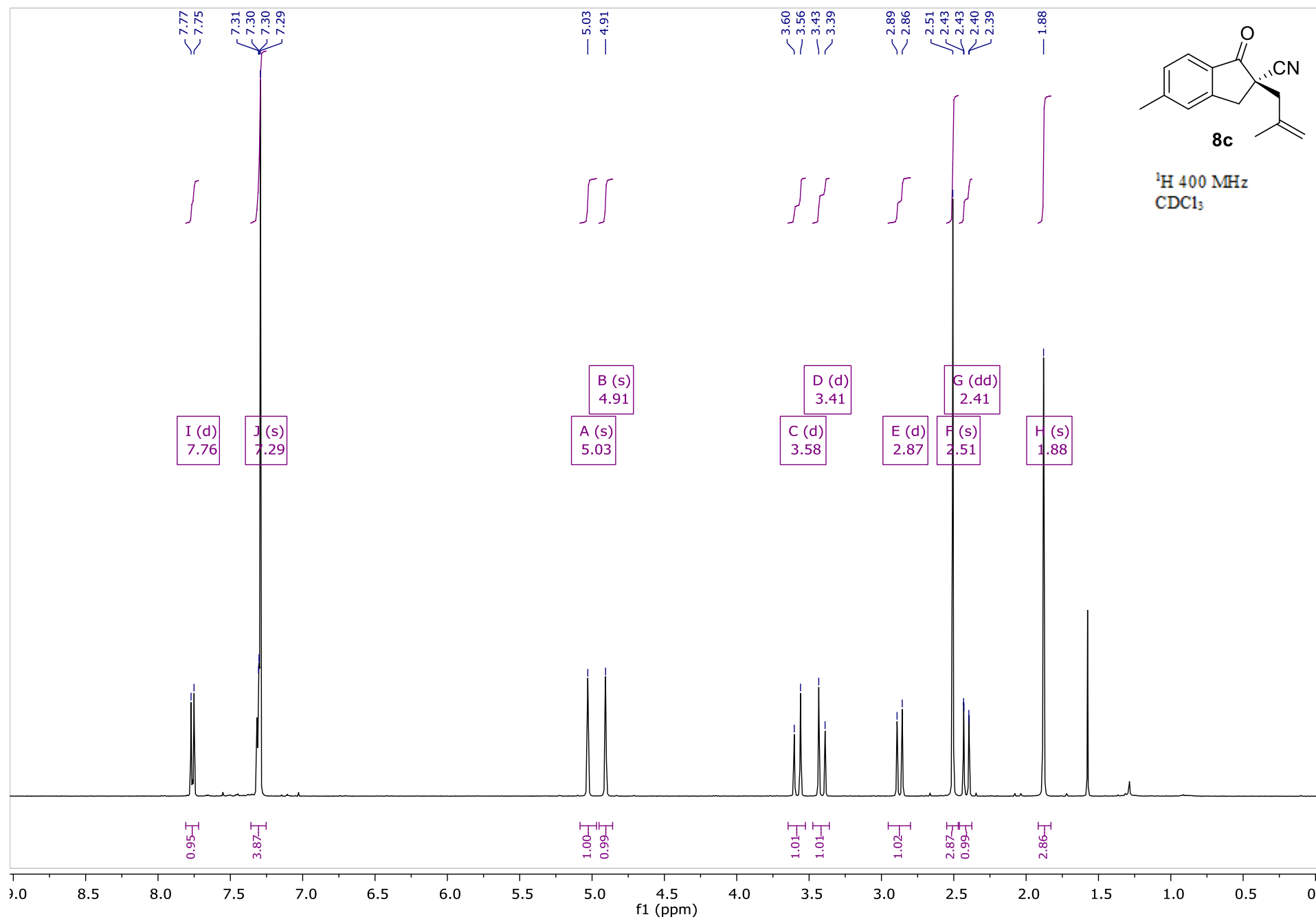


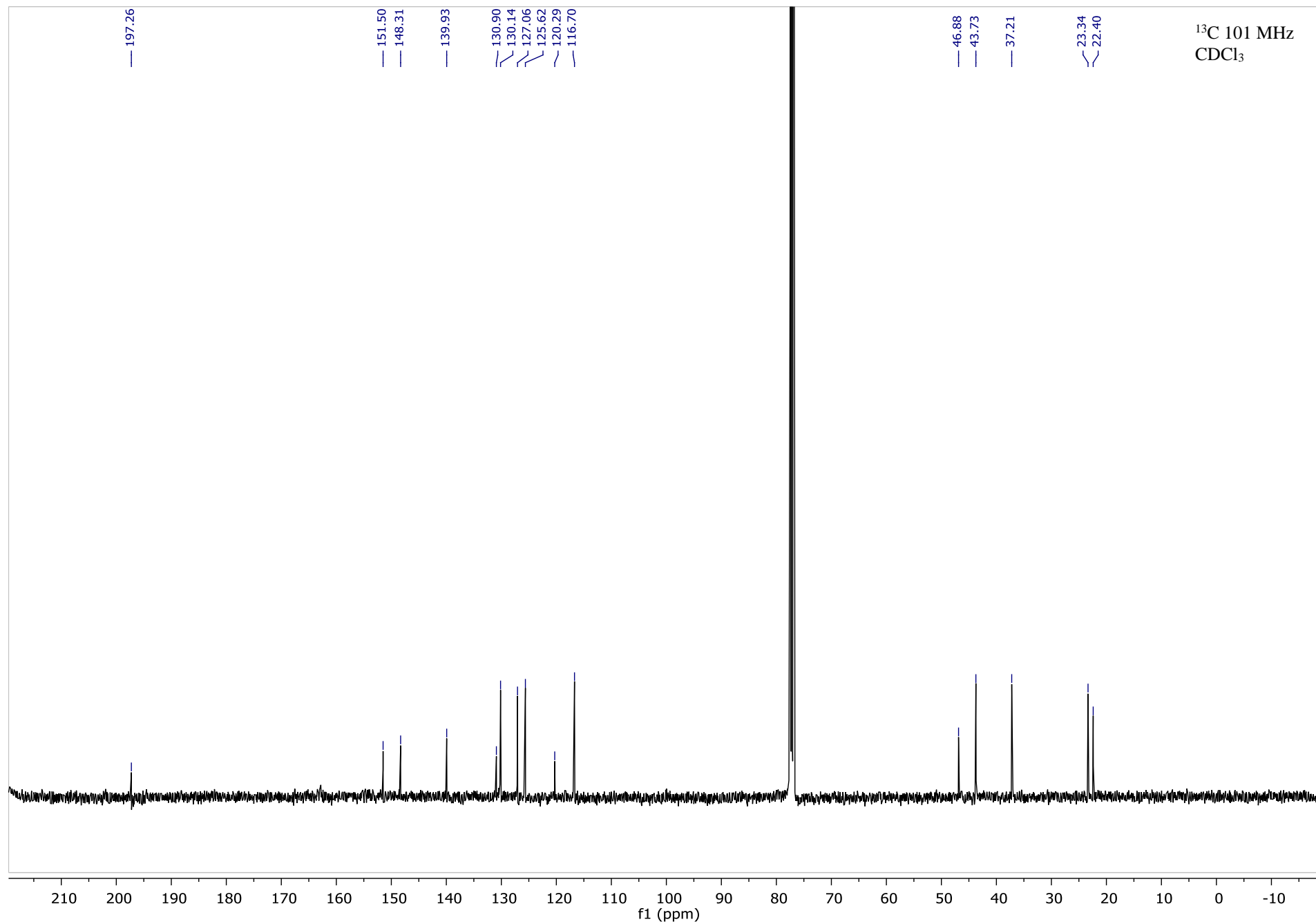


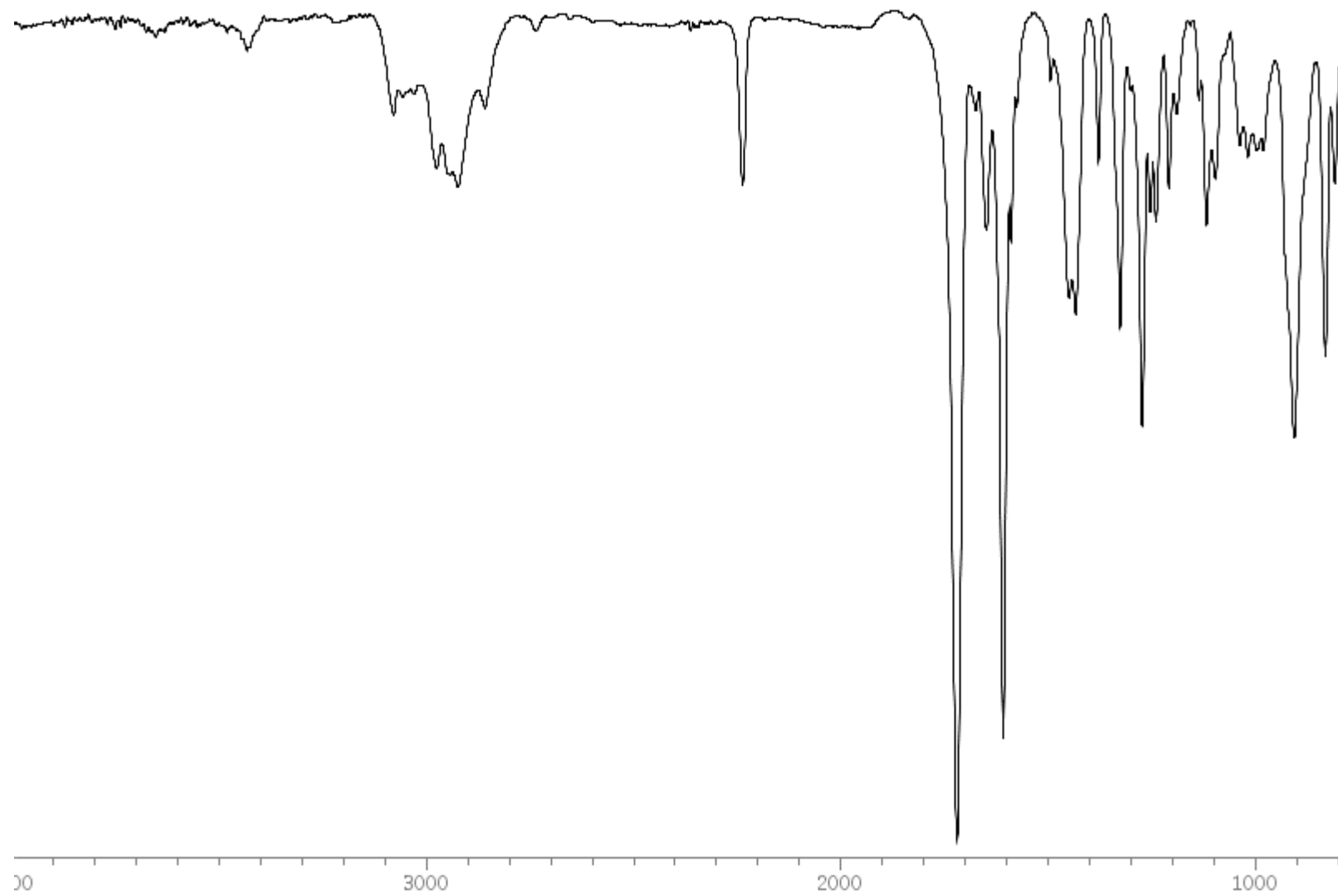


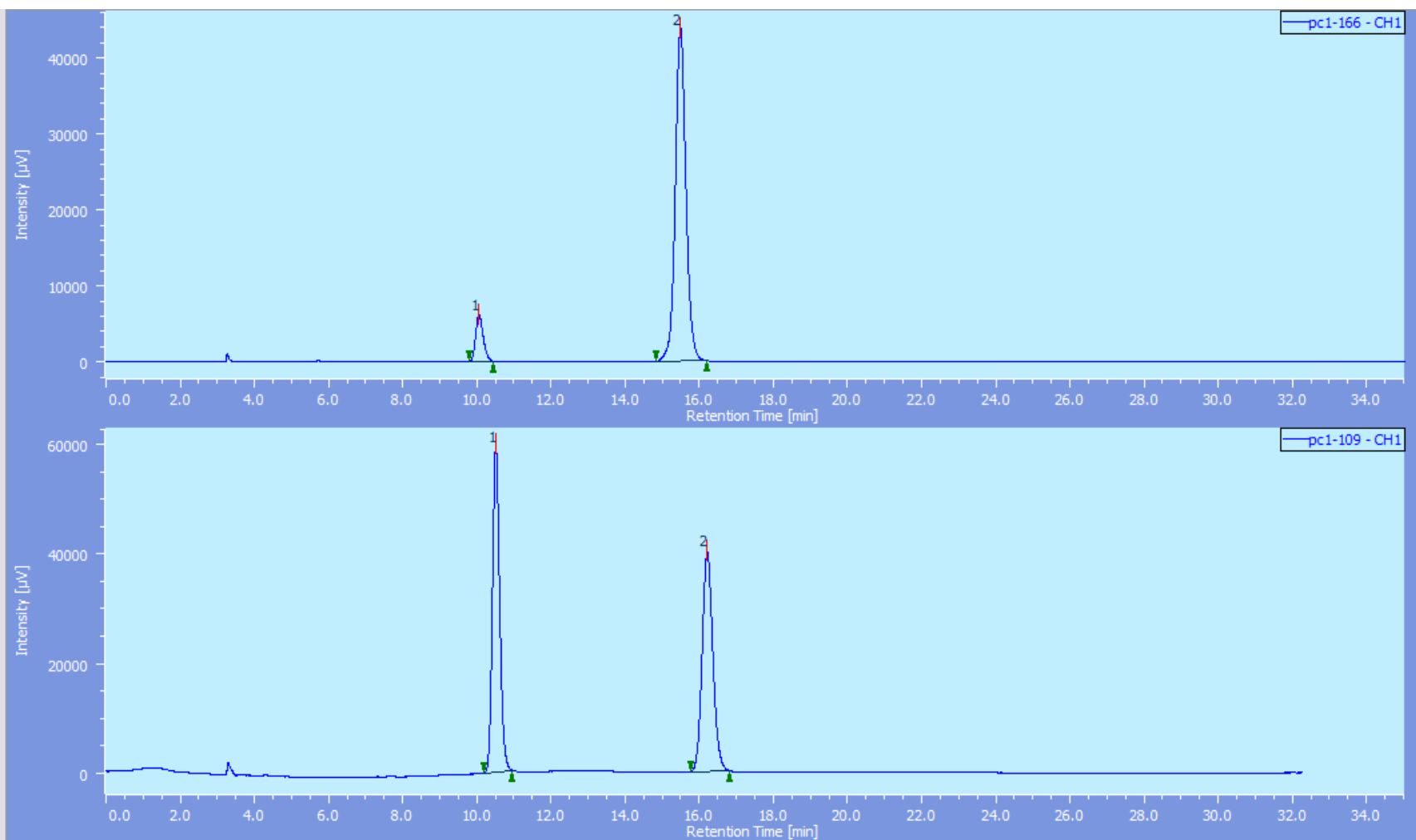






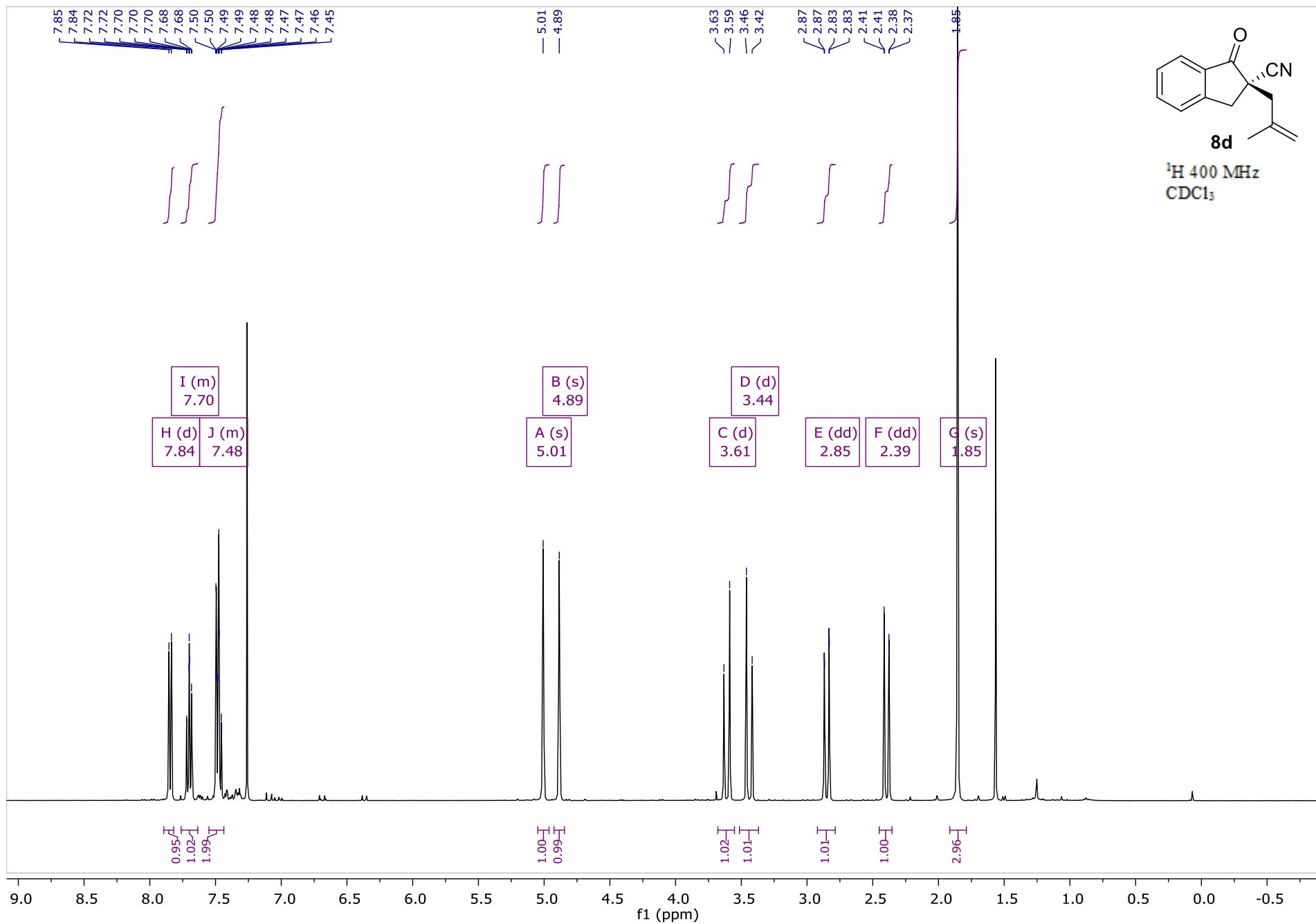


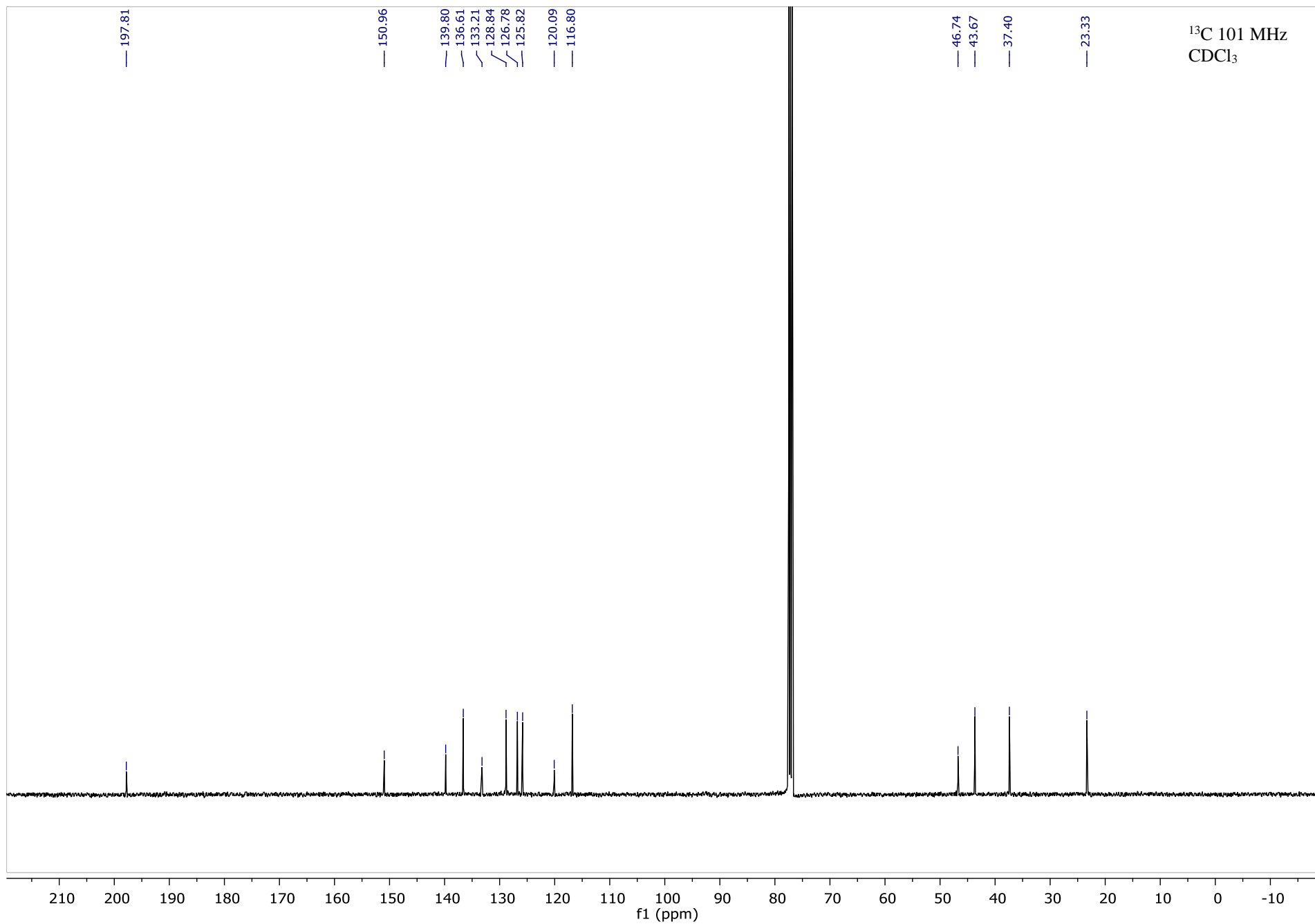


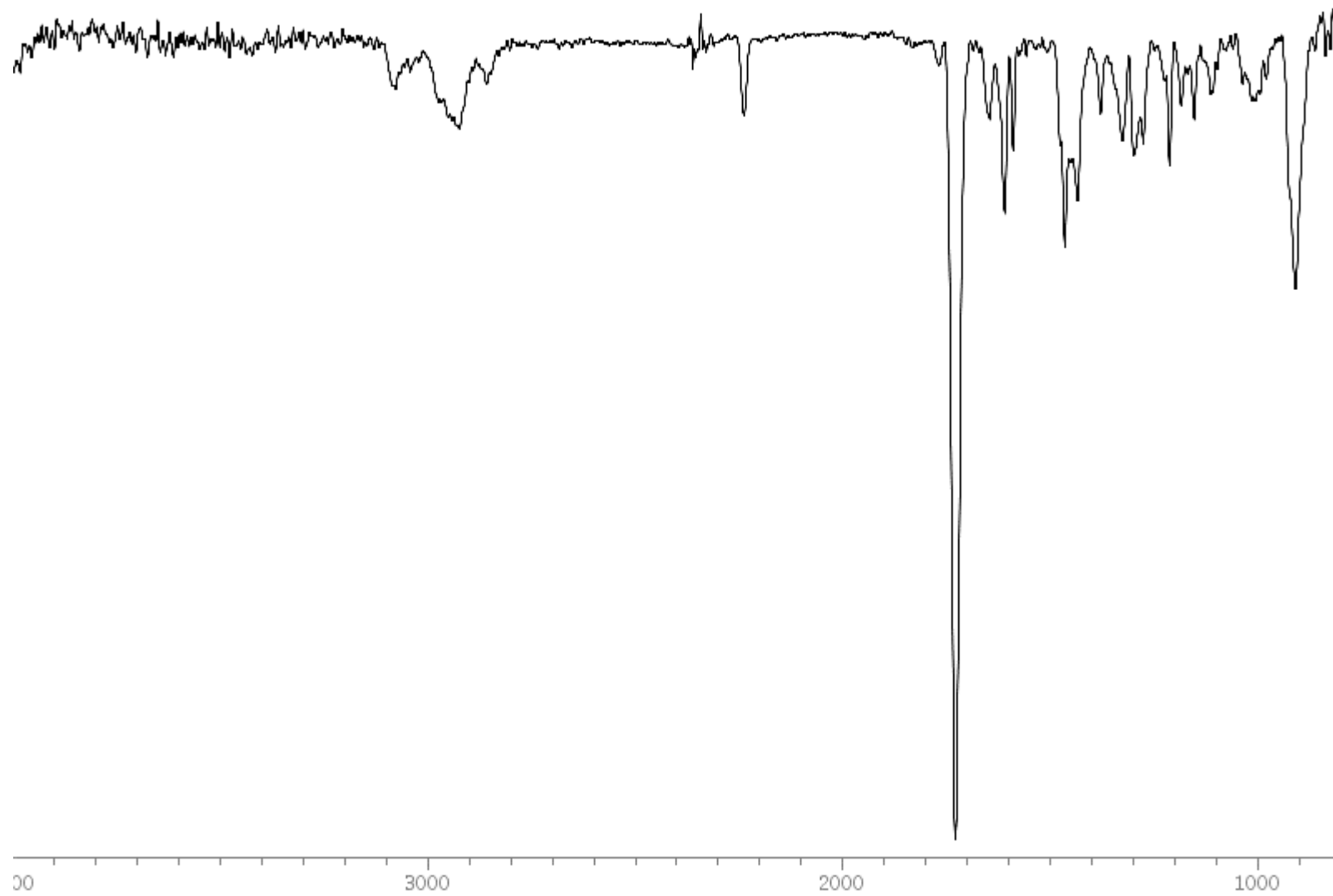


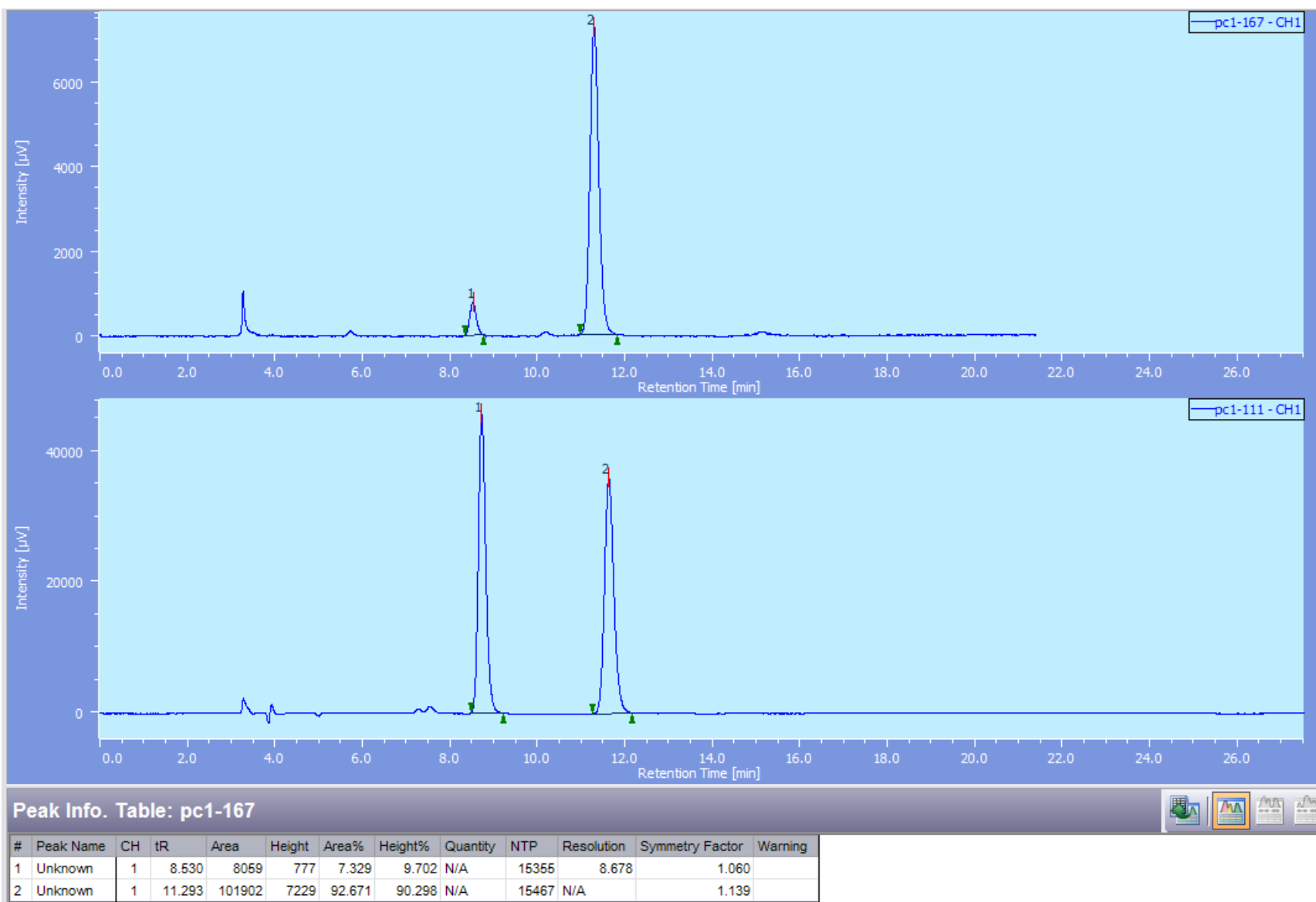
Peak Info. Table: pc1-166

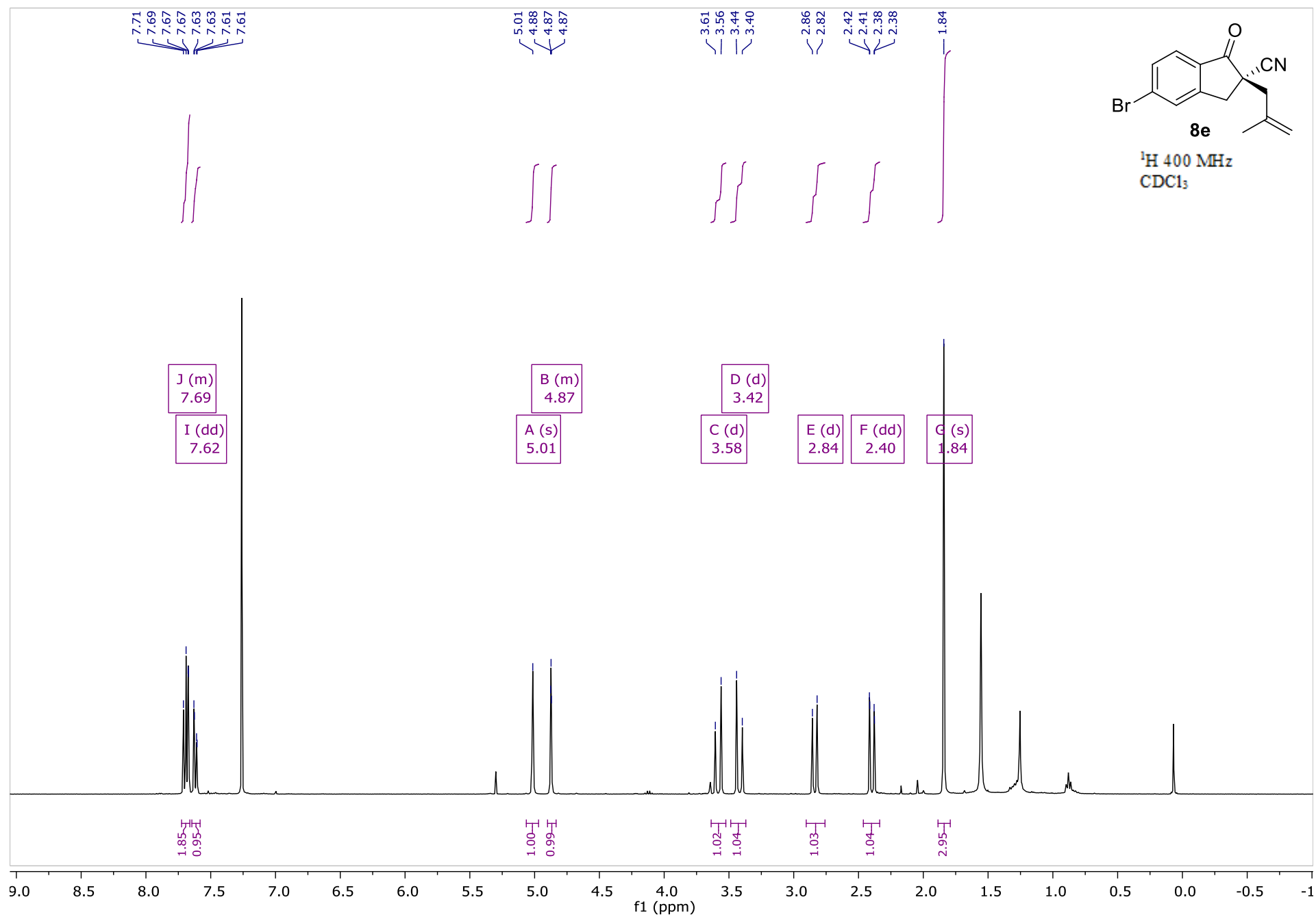
| # | Peak Name | CH | tR | Area | Height | Area% | Height% | Quantity | NTP | Resolution | Symmetry Factor | Warning |
|---|-----------|----|--------|--------|--------|--------|---------|----------|-------|------------|-----------------|---------|
| 1 | Unknown | 1 | 10.047 | 86167 | 6108 | 9.016 | 12.269 | N/A | 11825 | 12.465 | 1.245 | |
| 2 | Unknown | 1 | 15.477 | 869561 | 43677 | 90.984 | 87.731 | N/A | 15087 | N/A | 1.068 | |

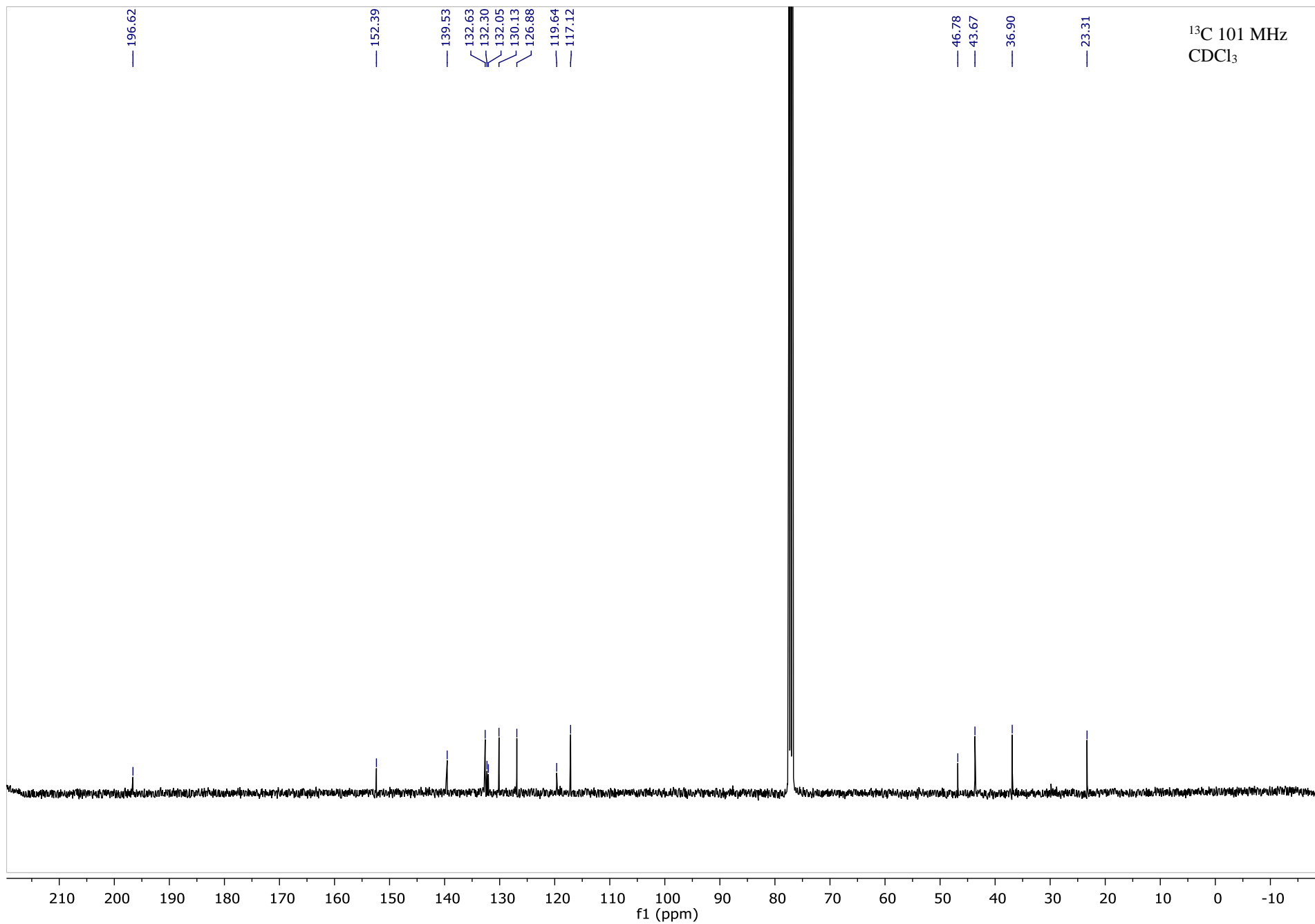


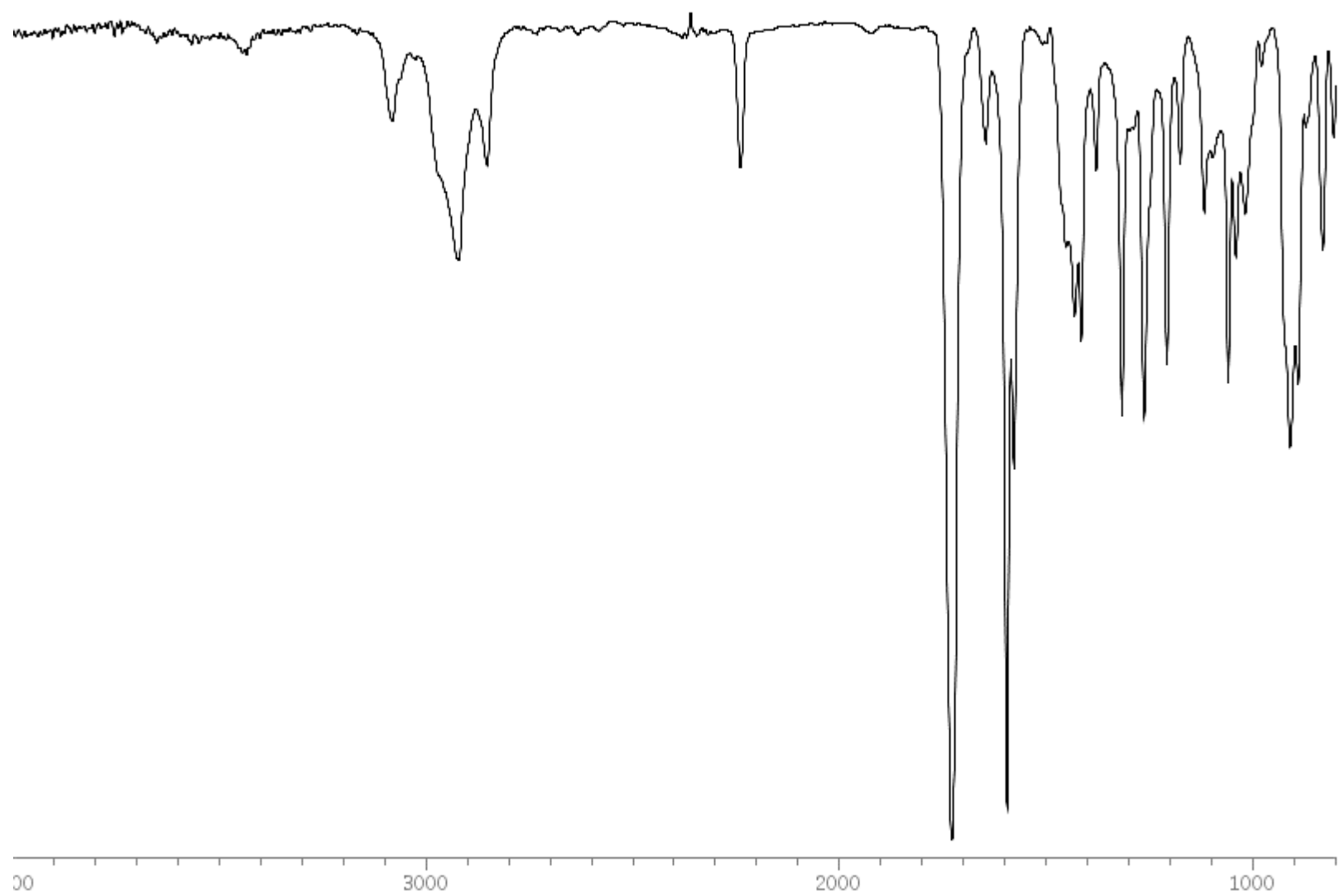


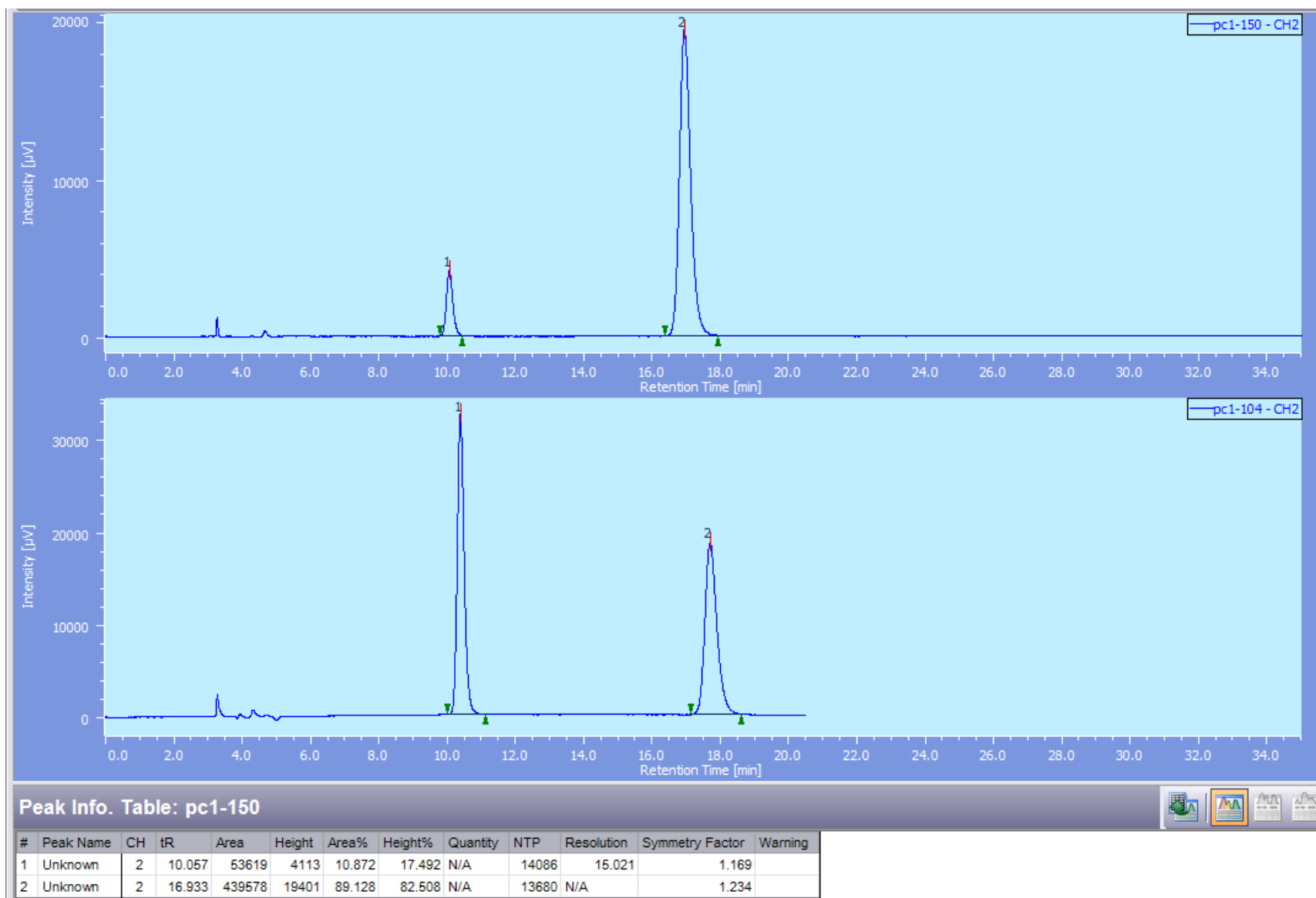


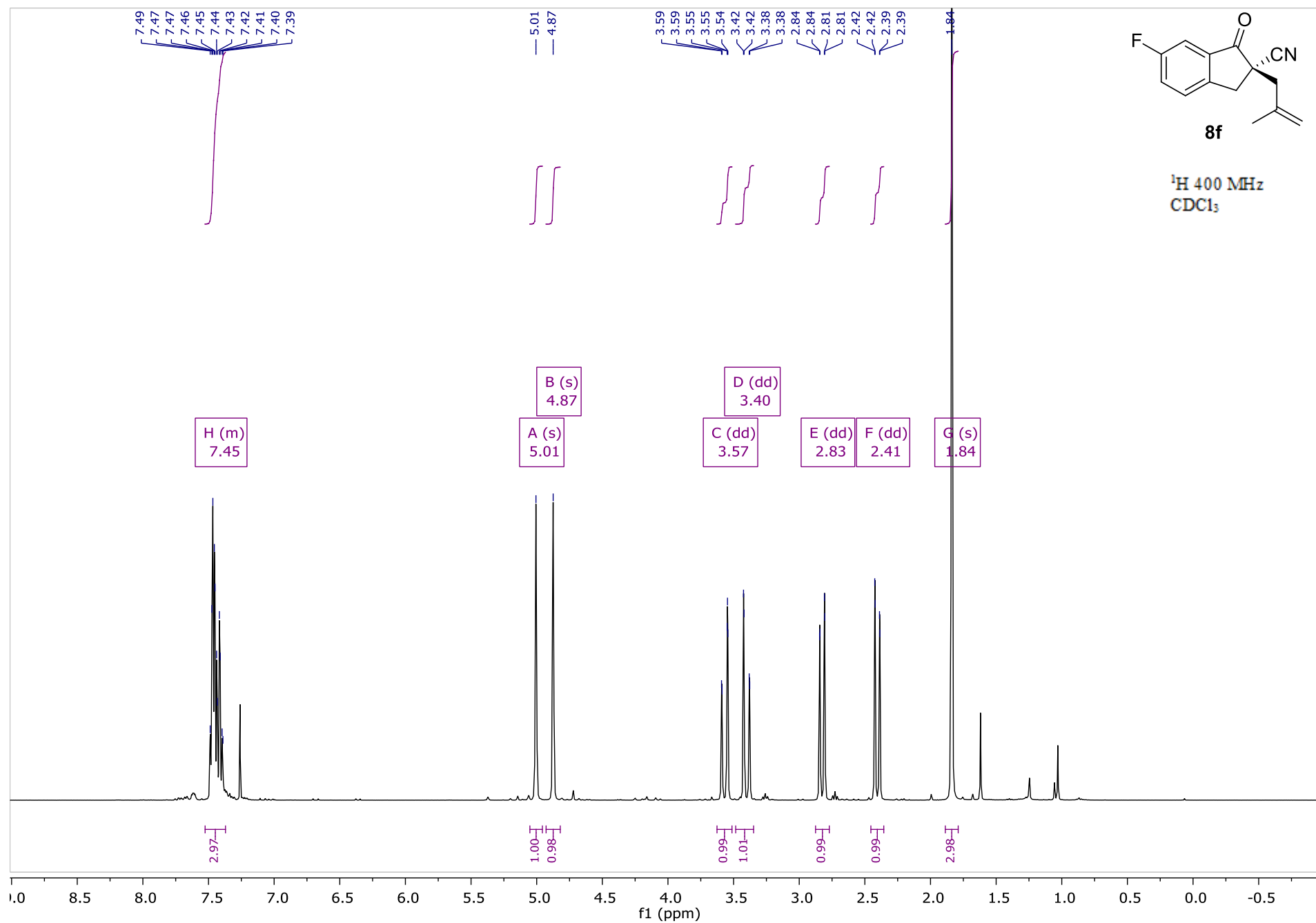


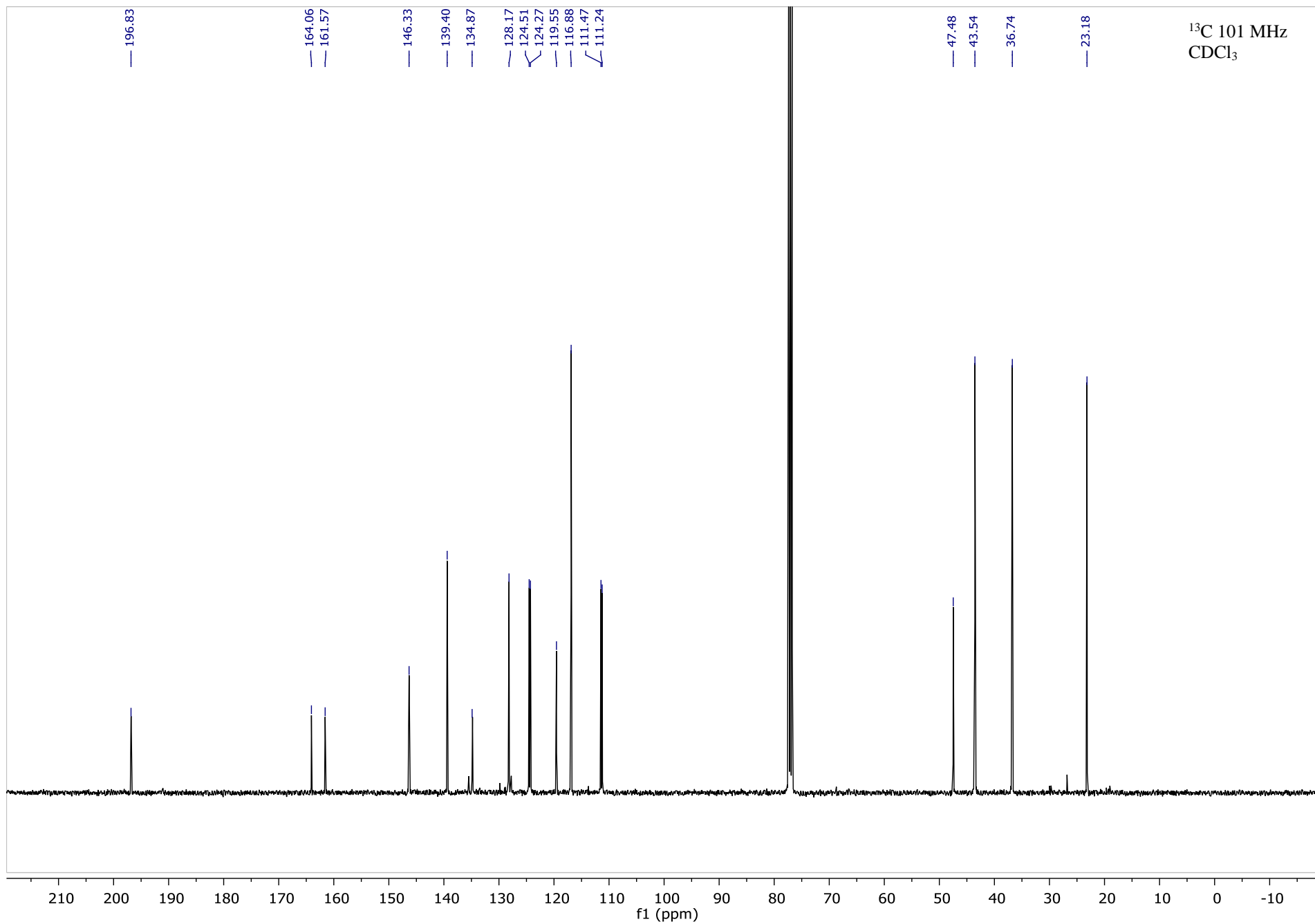


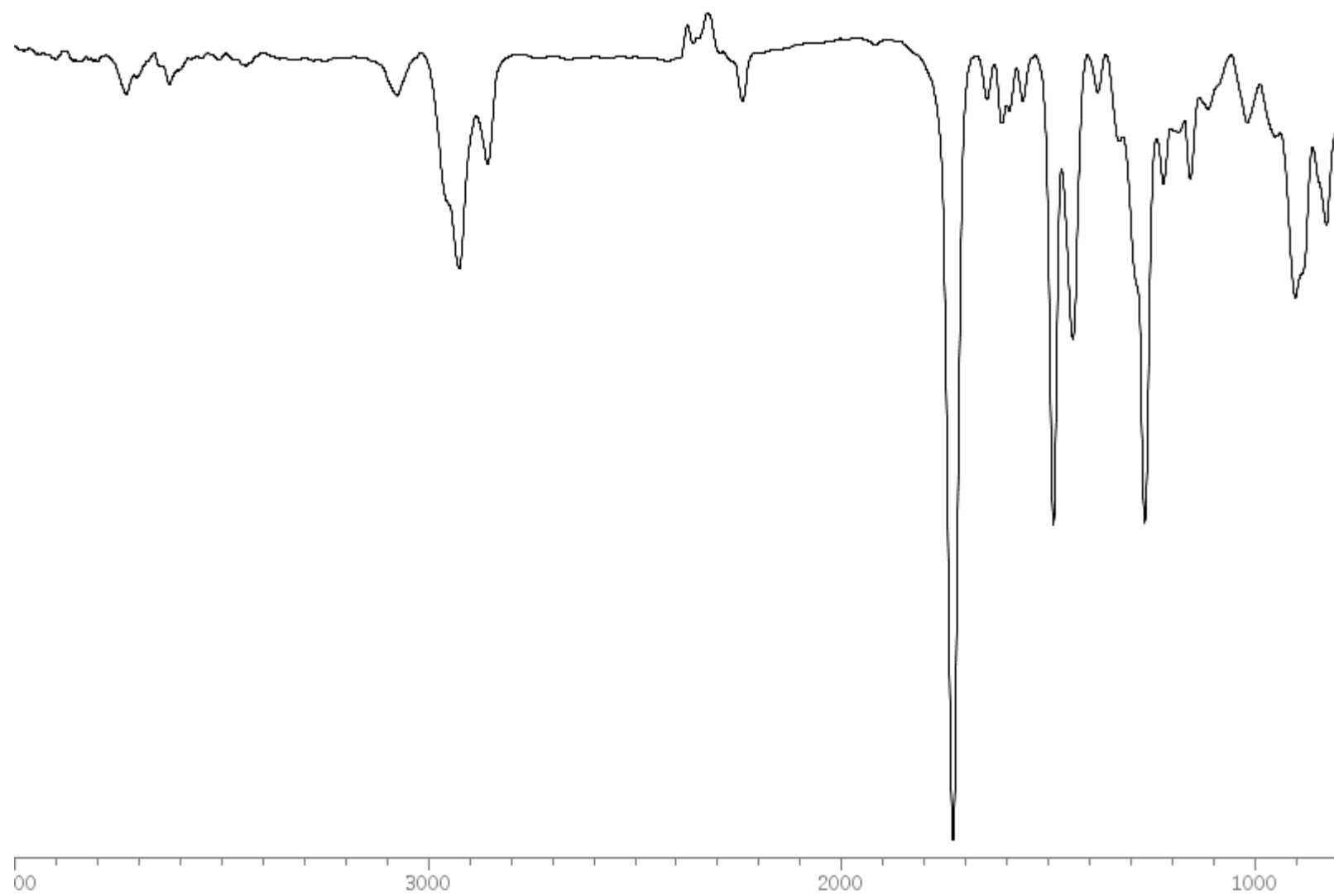


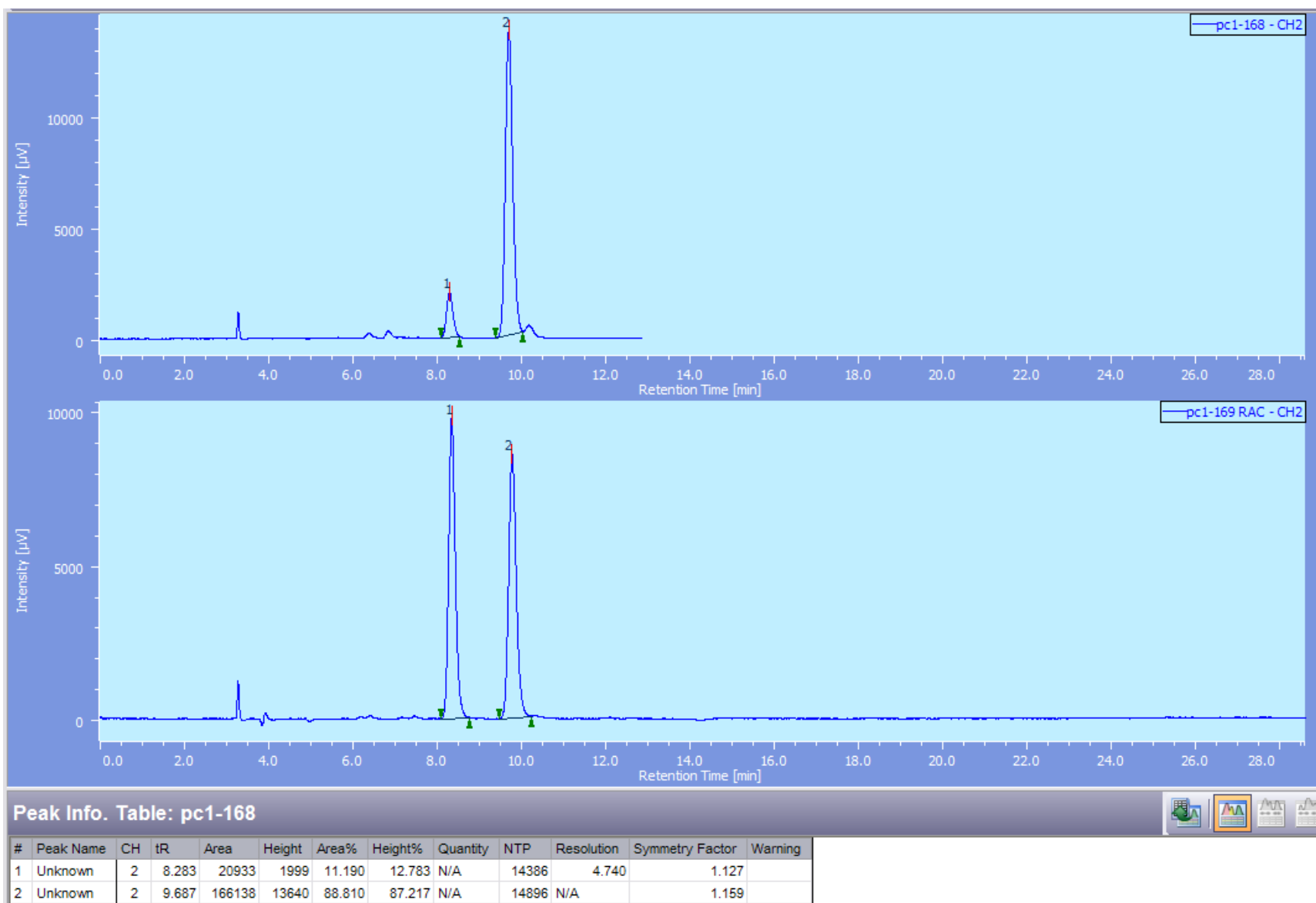


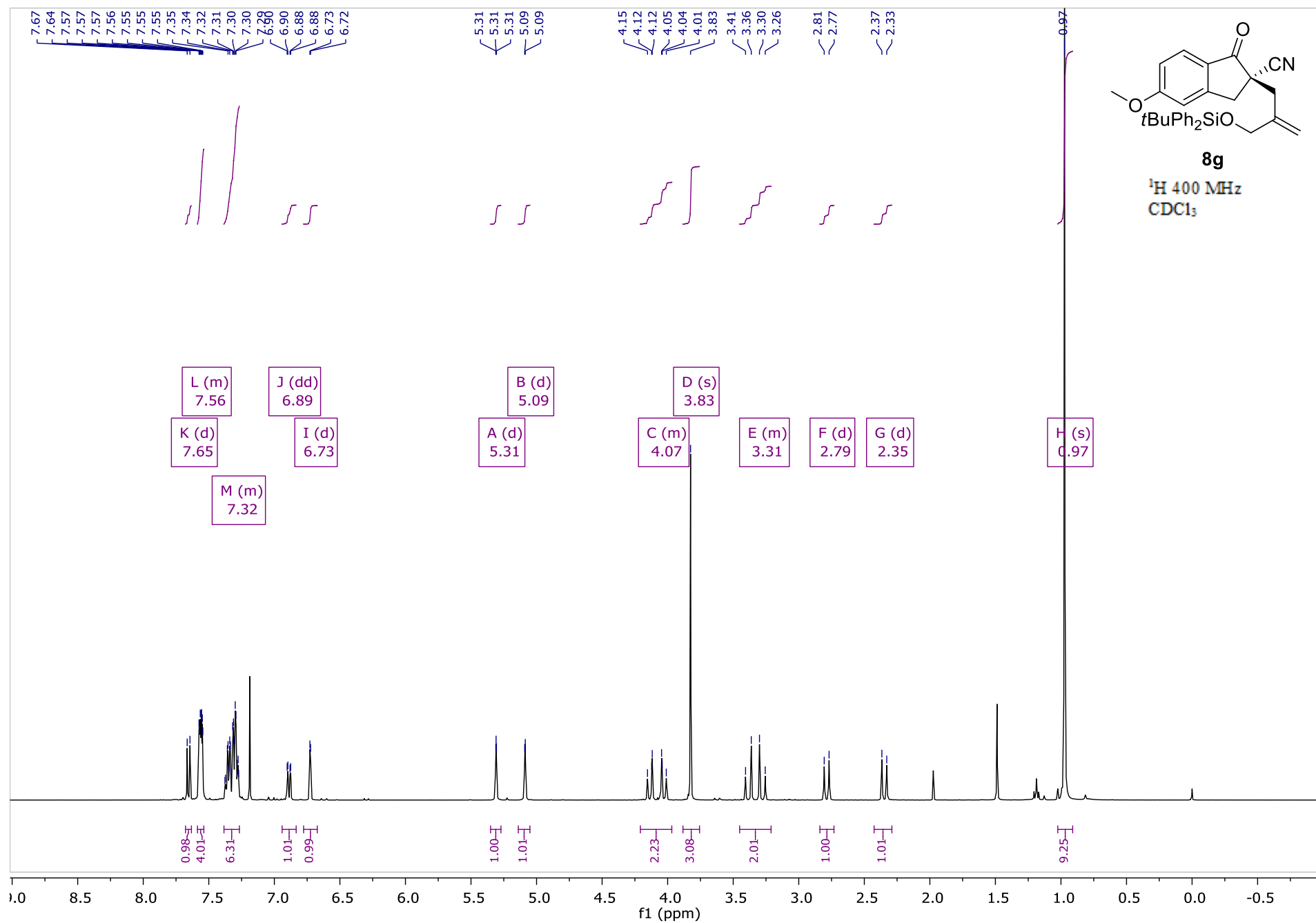


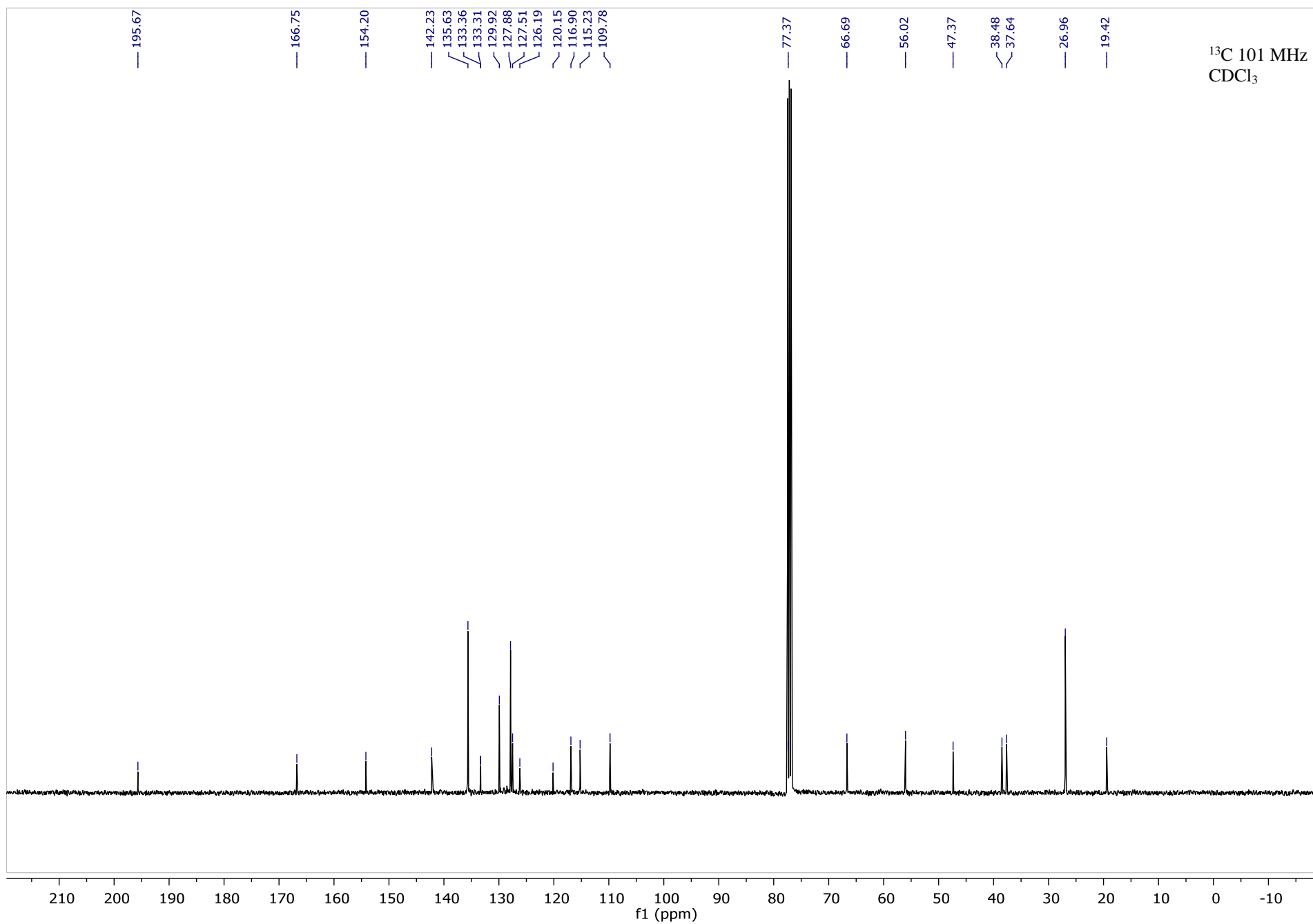


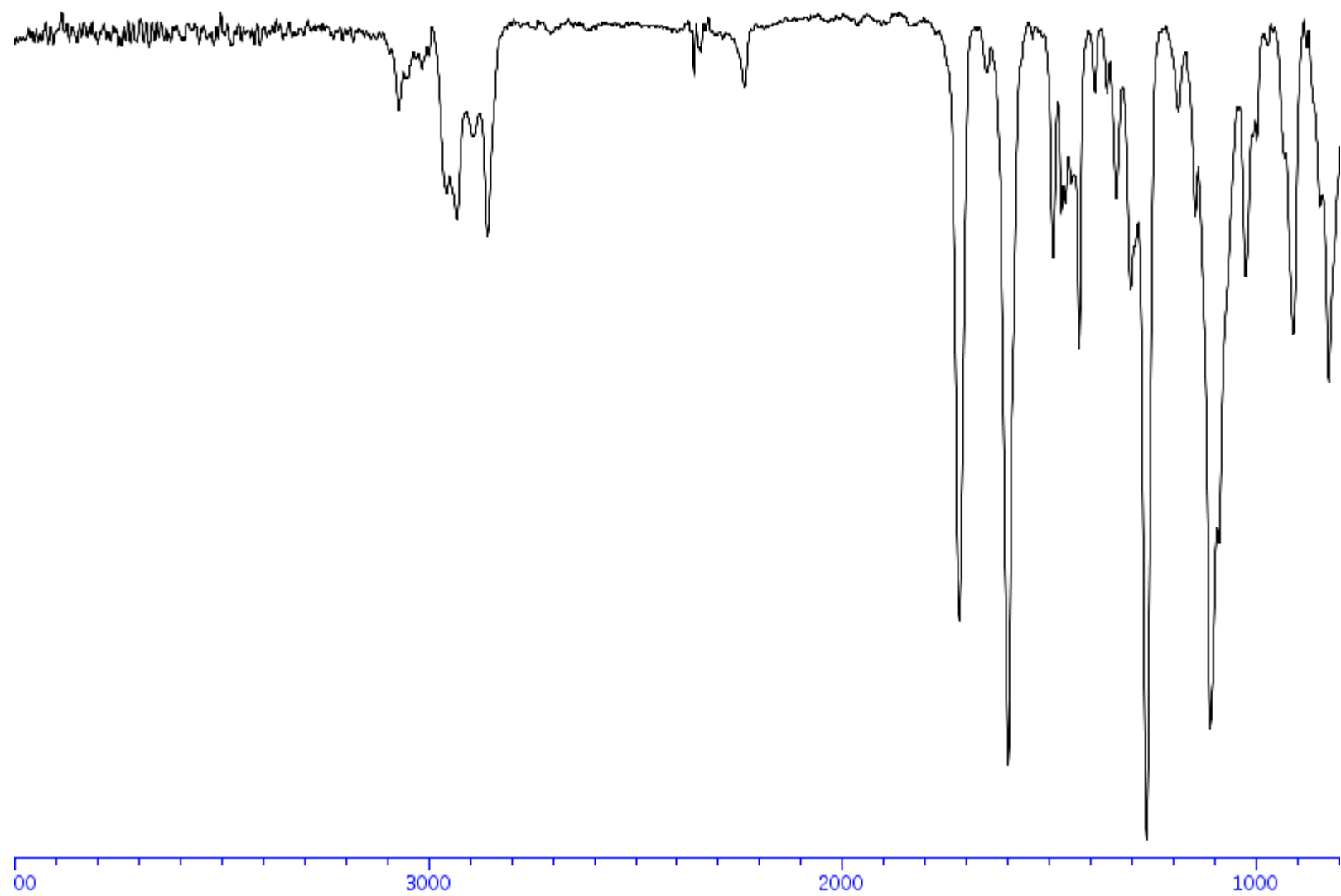




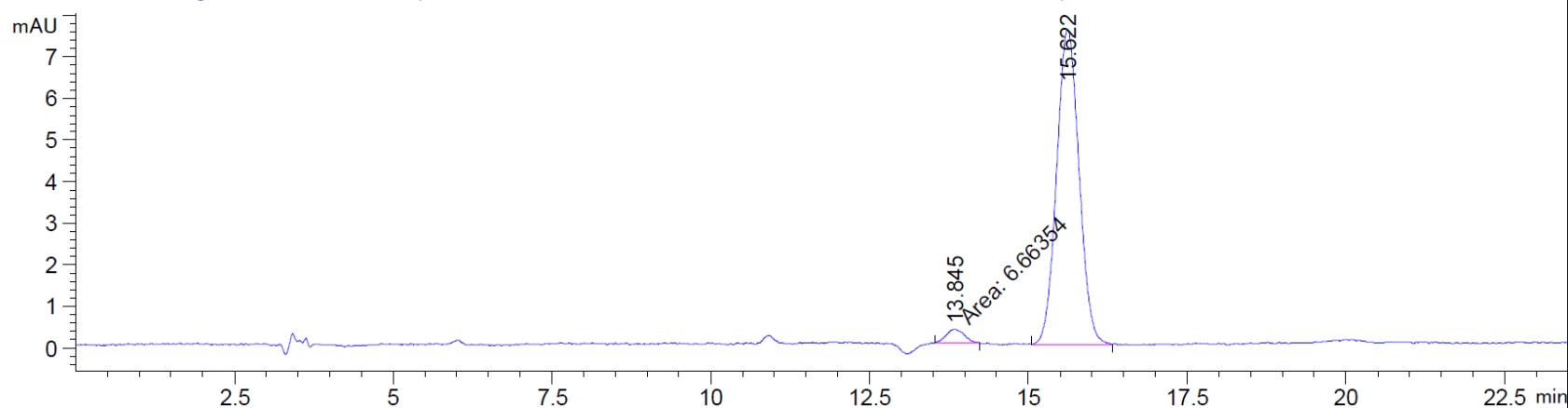




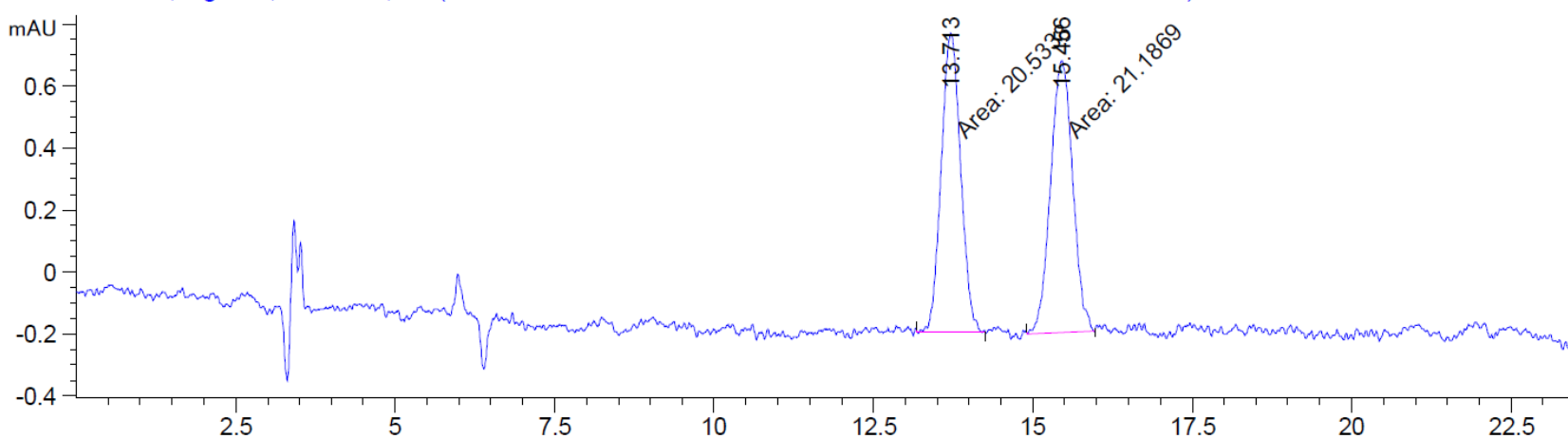




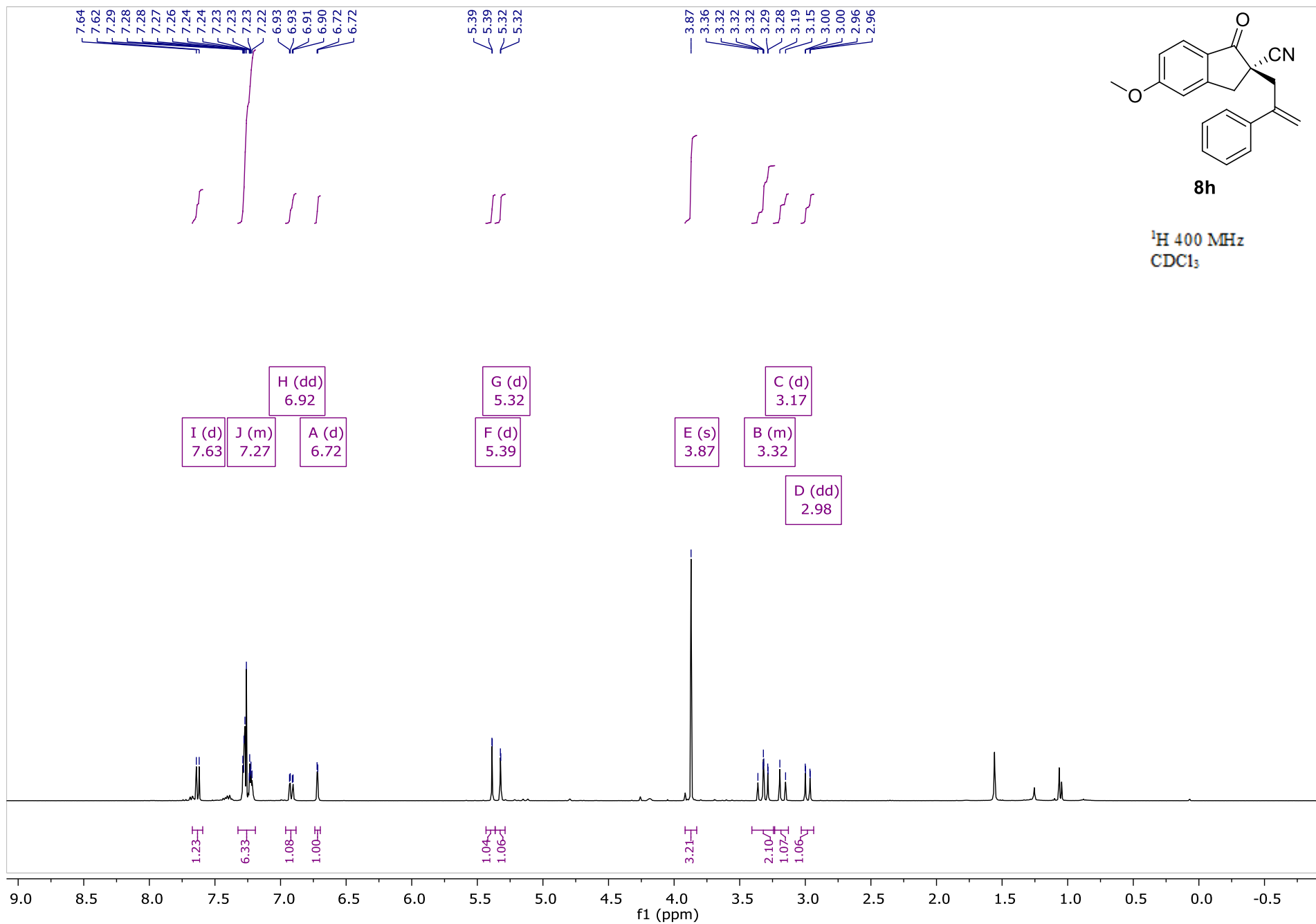
DAD1 A, Sig=254,4 Ref=360,100 (DG\PC-1-179-IC80-25 2015-07-02 14-07-28\PC1-179-IC80-25.D)

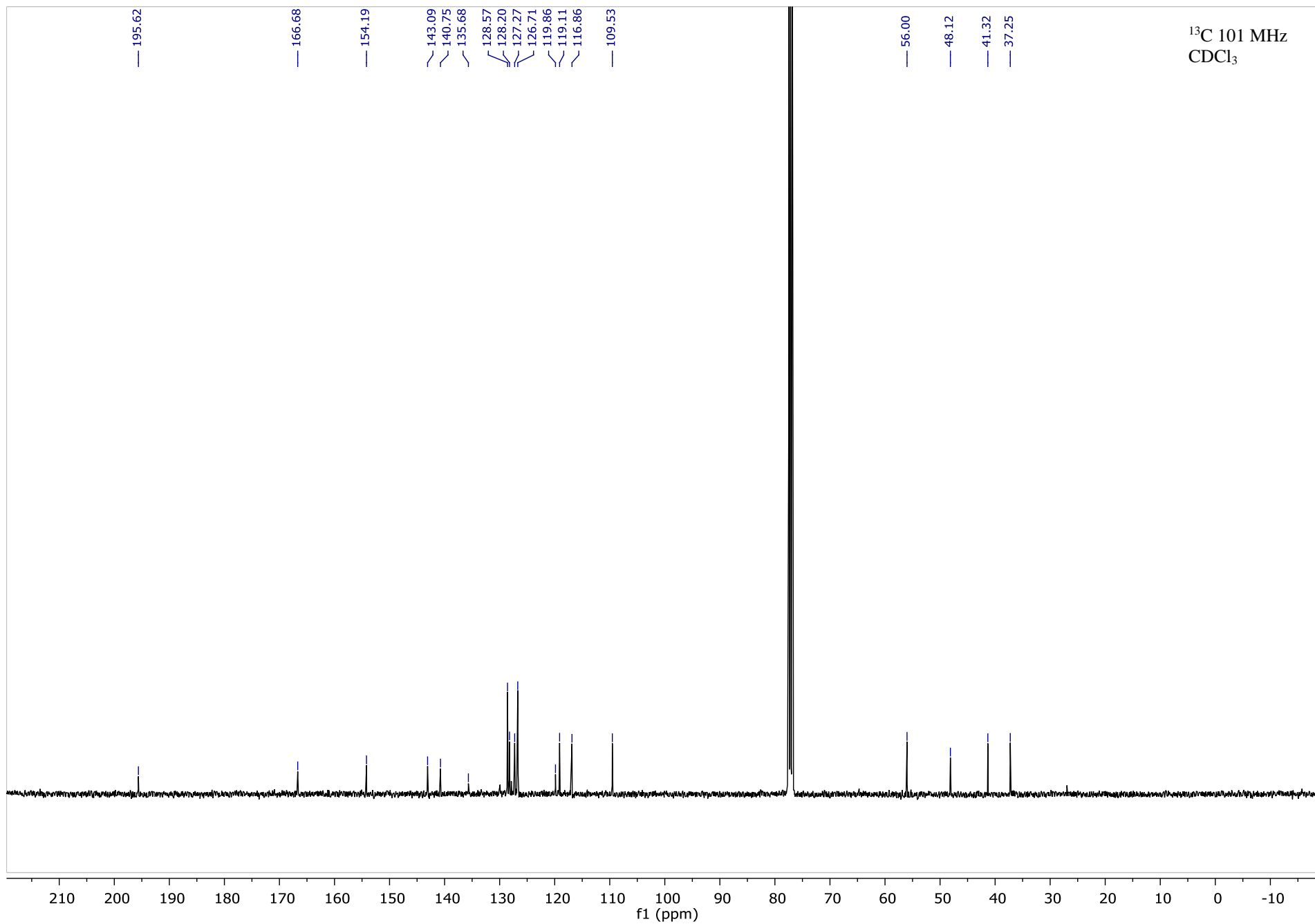


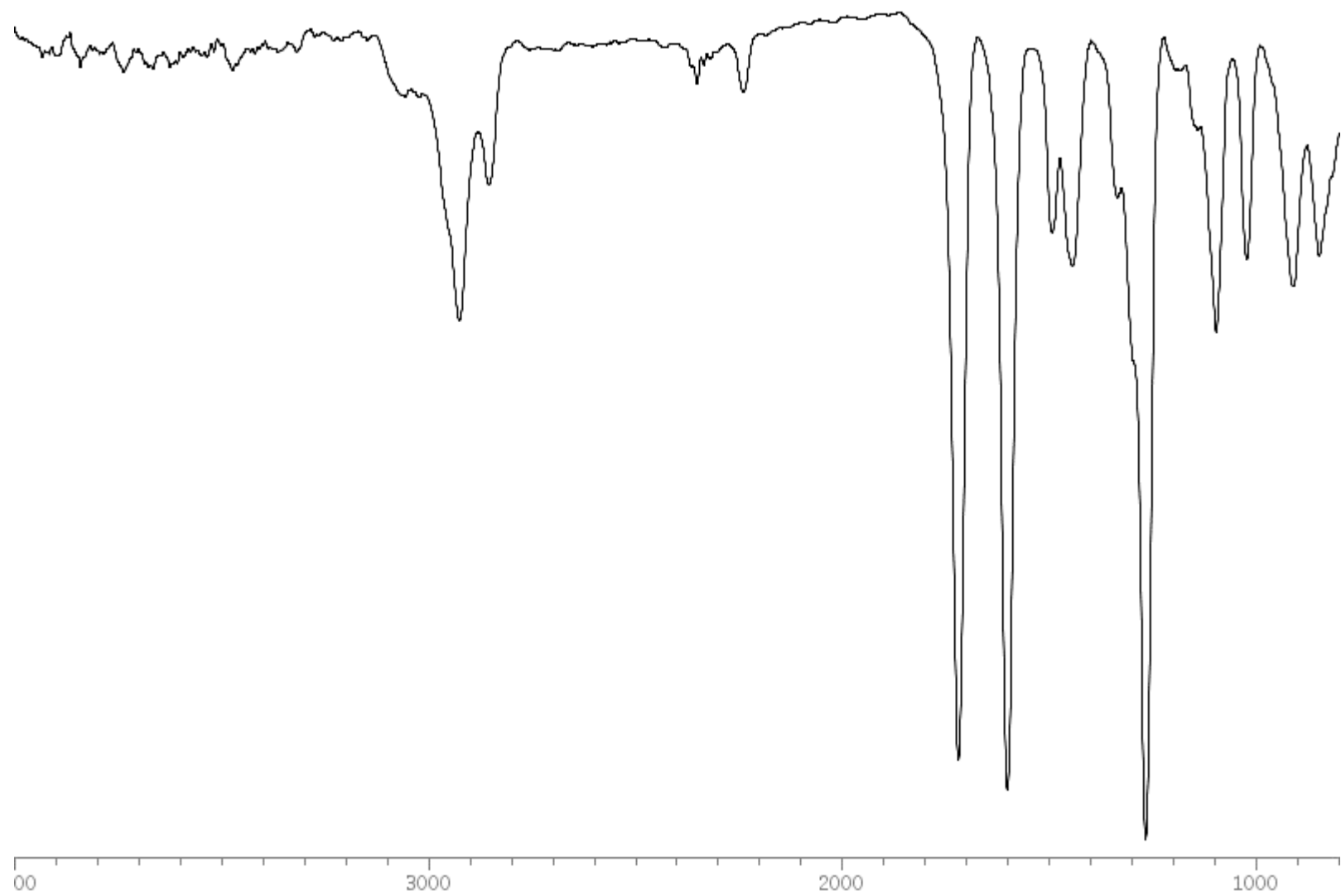
DAD1 A, Sig=254,4 Ref=360,100 (DG\PC-1-178-SCREENING 2015-07-02 11-44-54\PC1-178-IC80-25.D)

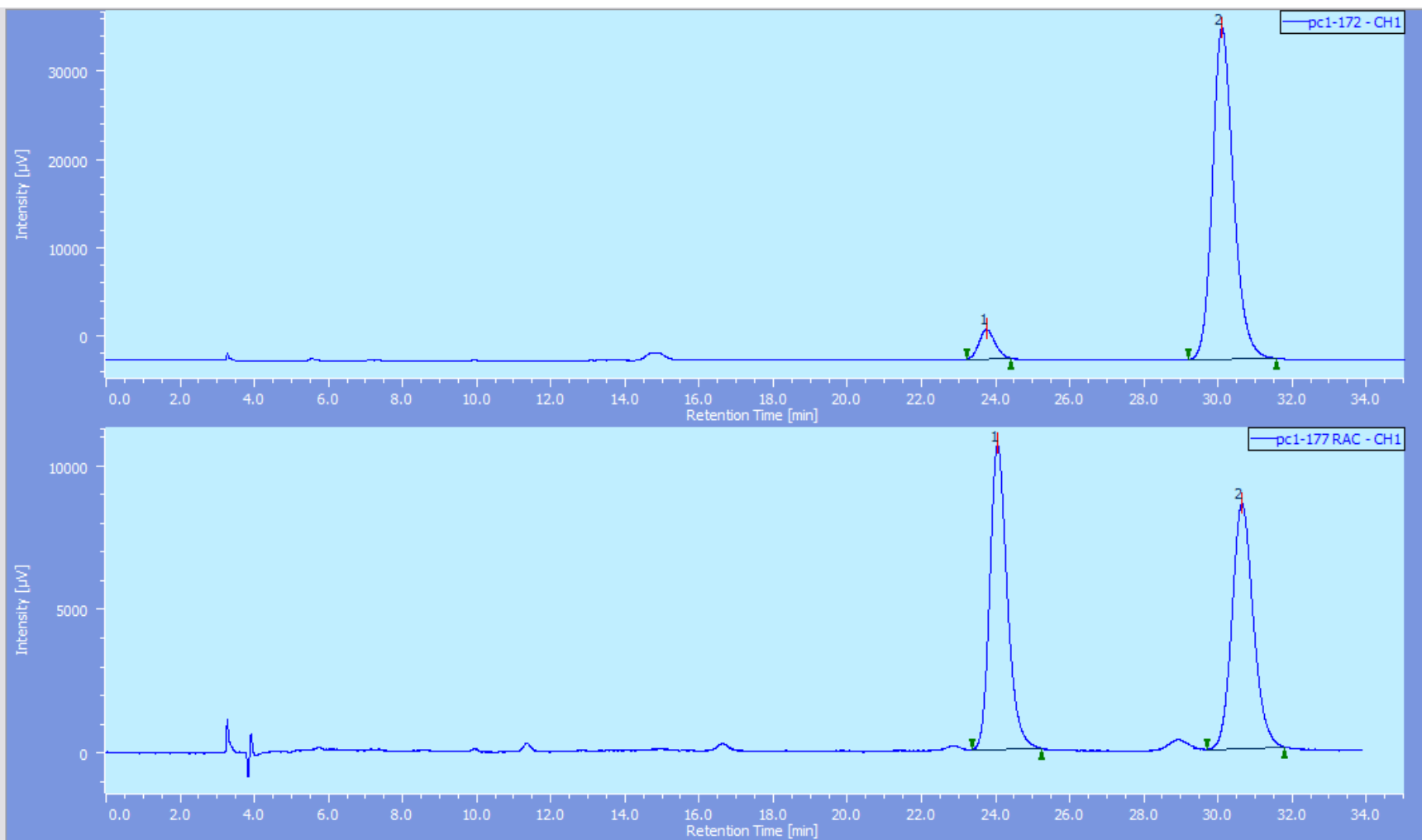


| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|--------|---------------|------|-------------|--------------|--------------|---------|
| 1 | 13.845 | MM | 0.3339 | 6.66354 | 3.32654e-1 | 3.4625 |
| 2 | 15.622 | BB | 0.3825 | 185.78767 | 7.56524 | 96.5375 |



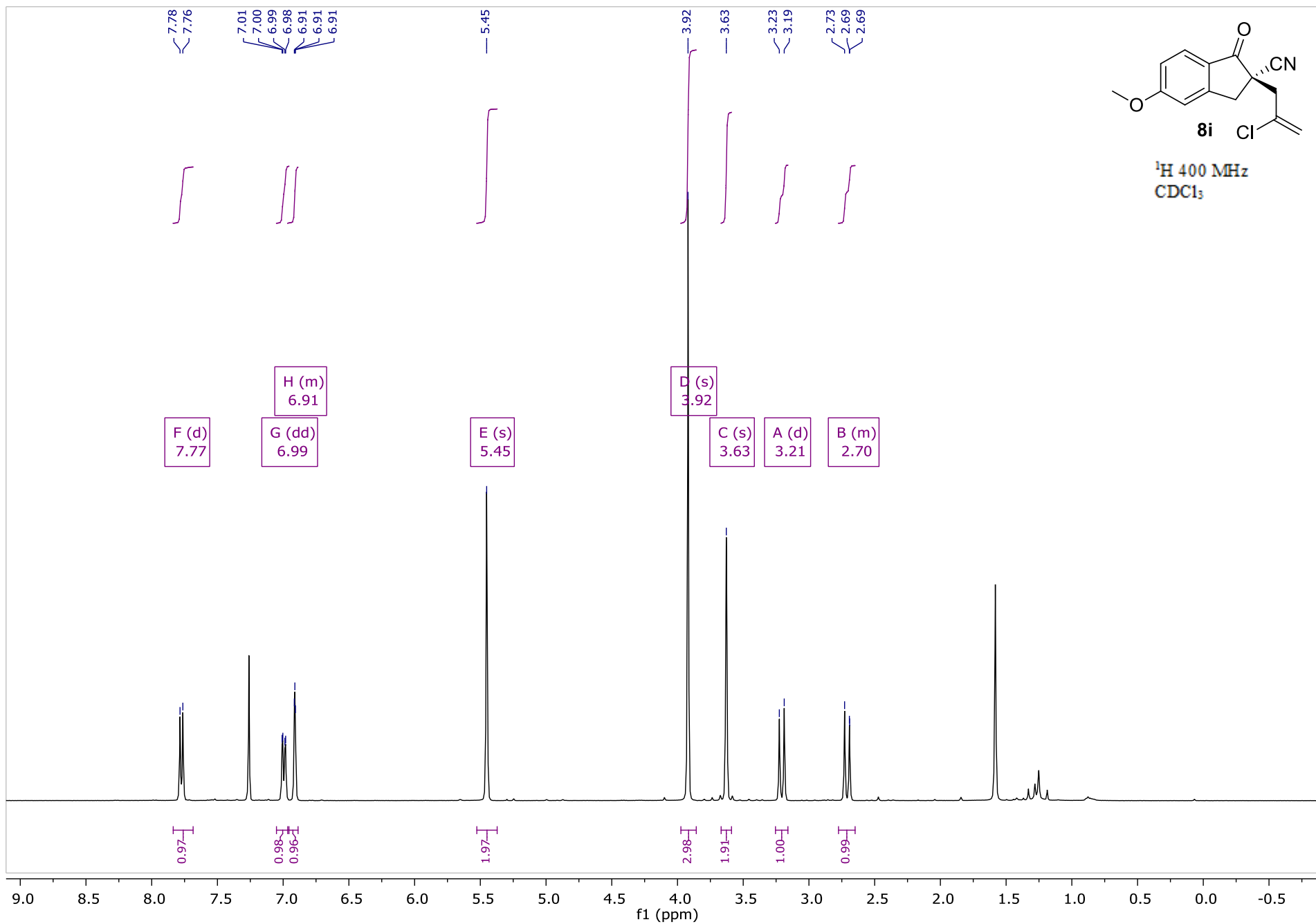


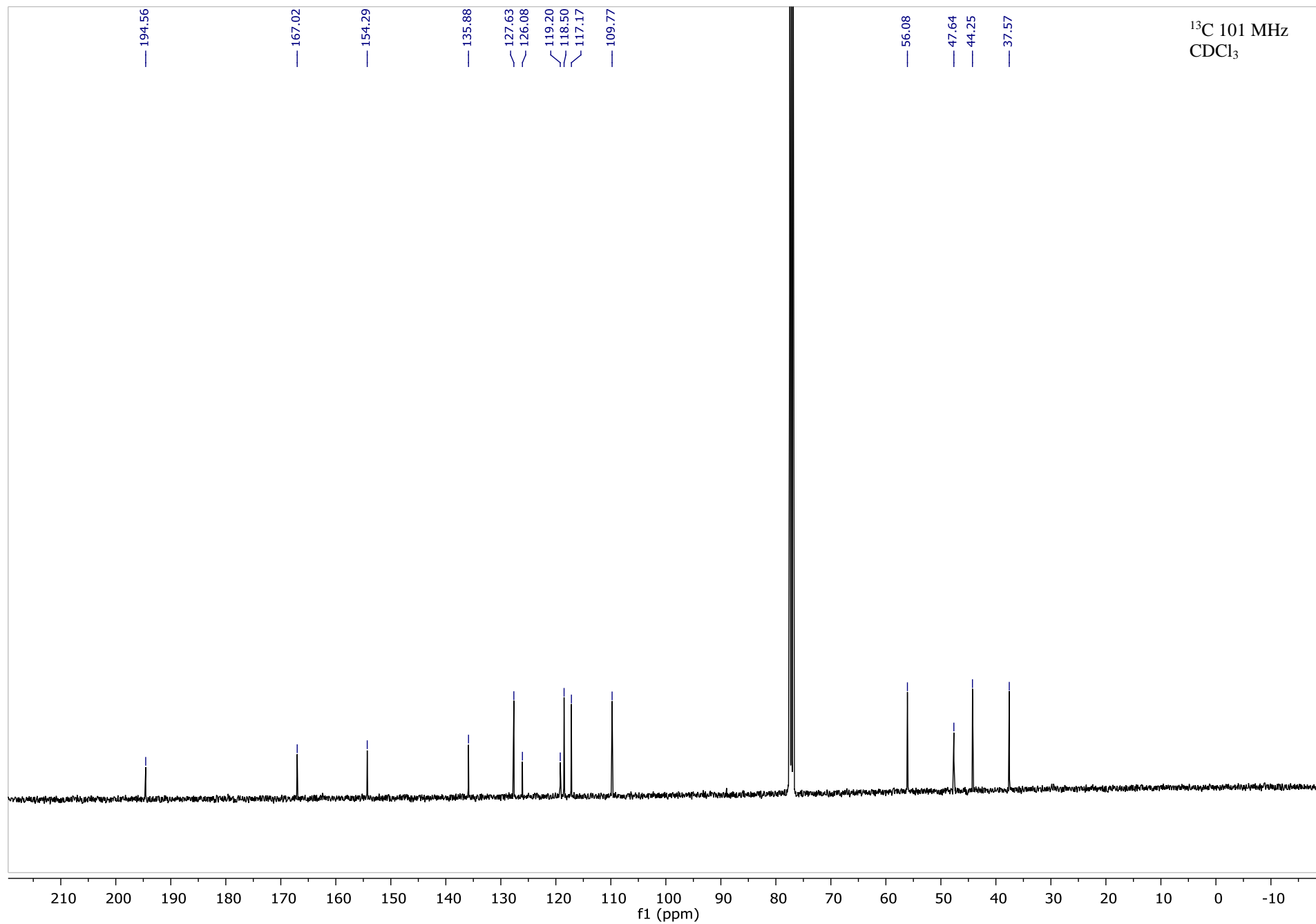


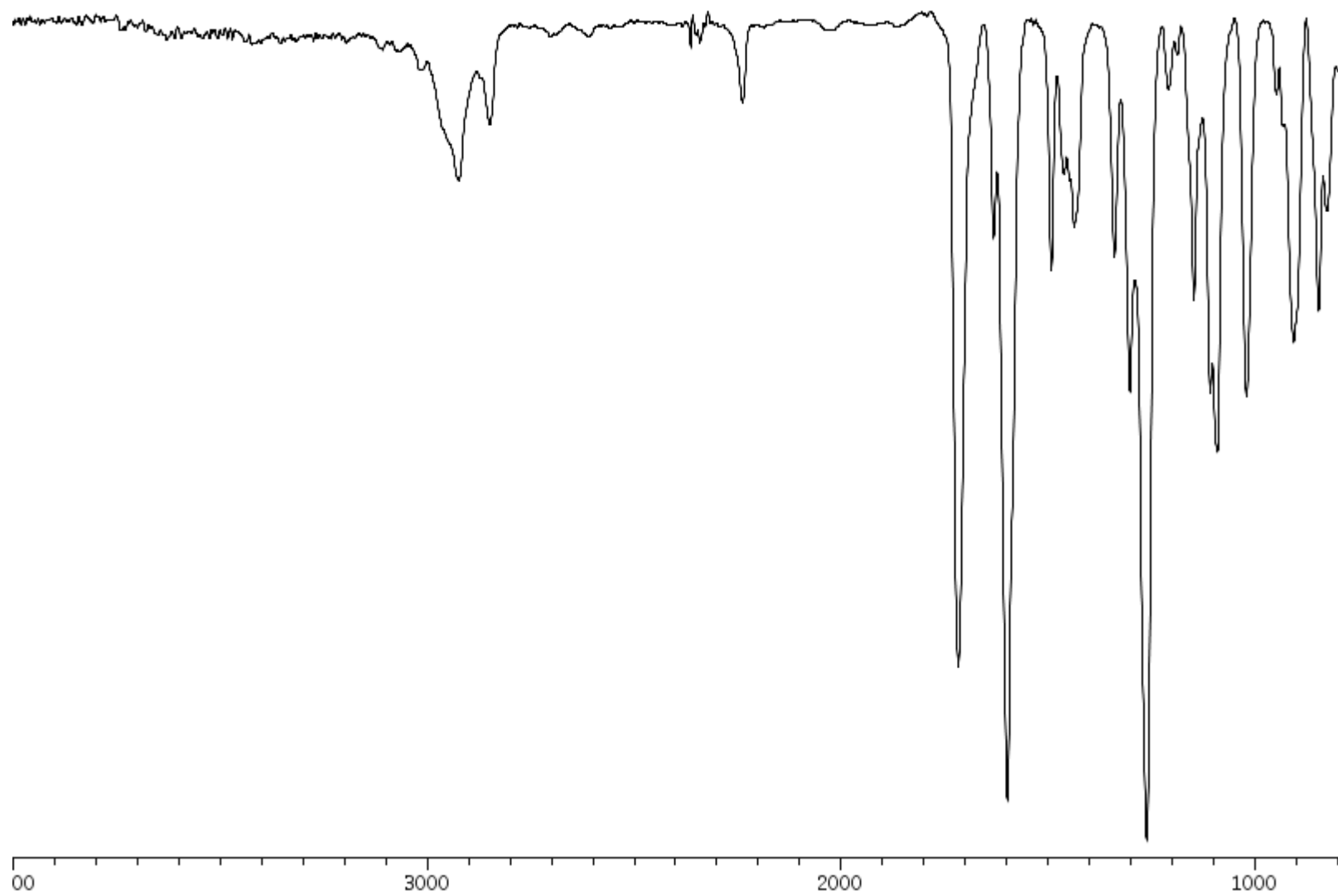


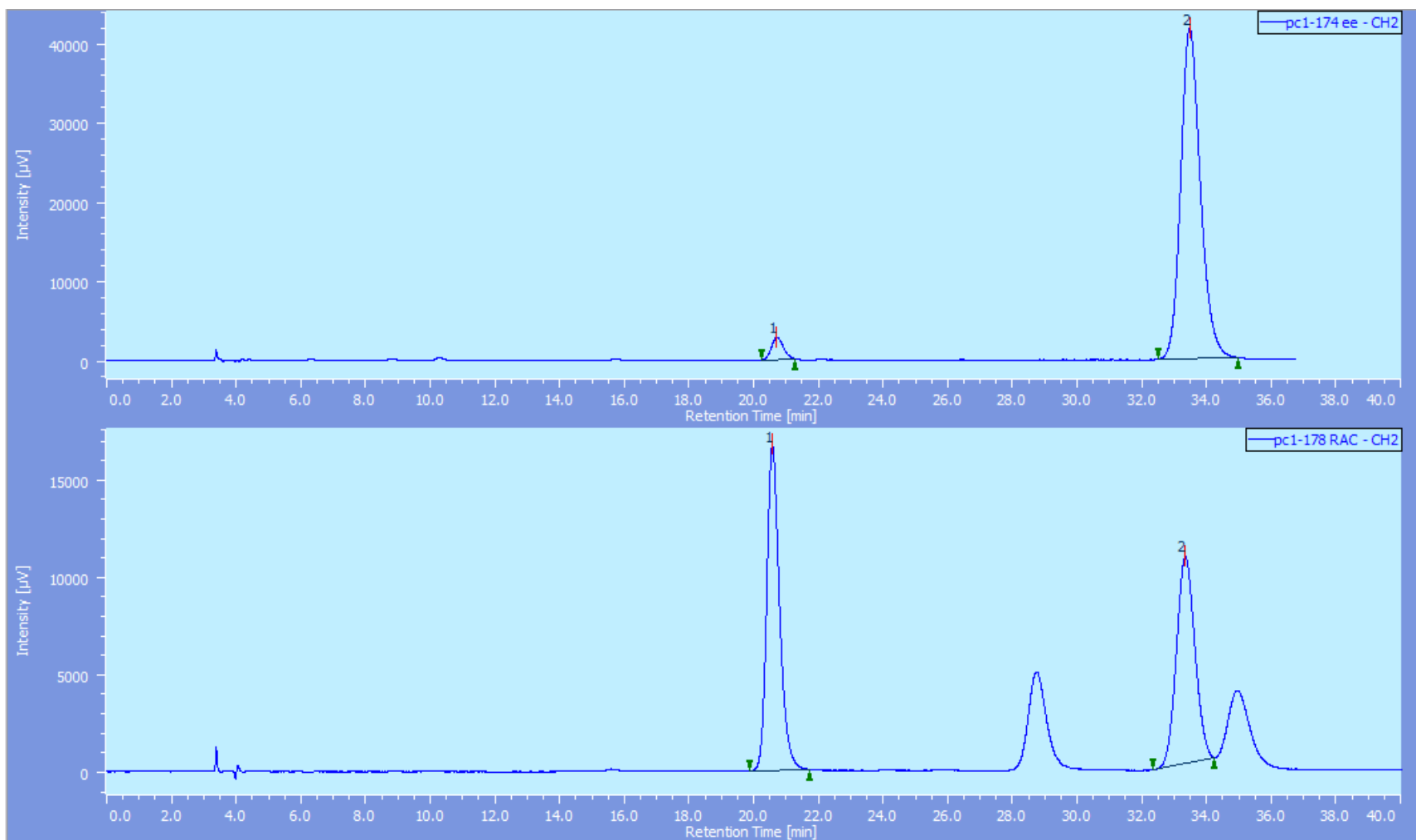
Peak Info. Table: pc1-172

| # | Peak Name | CH | tR | Area | Height | Area% | Height% | Quantity | NTP | Resolution | Symmetry Factor | Warning |
|---|-----------|----|--------|---------|--------|--------|---------|----------|-------|------------|-----------------|---------|
| 1 | Unknown | 1 | 23.737 | 98363 | 3302 | 6.247 | 8.100 | N/A | 14326 | 7.063 | 1.116 | |
| 2 | Unknown | 1 | 30.080 | 1476206 | 37466 | 93.753 | 91.900 | N/A | 14257 | N/A | 1.202 | |









Peak Info. Table: pc1-174 ee

| # | Peak Name | CH | tR | Area | Height | Area% | Height% | Quantity | NTP | Resolution | Symmetry Factor | Warning |
|---|-----------|----|--------|---------|--------|--------|---------|----------|-------|------------|-----------------|---------|
| 1 | Unknown | 2 | 20.697 | 70907 | 2764 | 3.886 | 6.237 | N/A | 14882 | 14.524 | 1.149 | |
| 2 | Unknown | 2 | 33.447 | 1753883 | 41555 | 96.114 | 93.763 | N/A | 15296 | N/A | 1.198 | |

